THE PATHOLOGY OF <u>MYCOPLASMA</u> <u>HYORHINIS</u> ARTHRITIS

EXPERIMENTALLY PRODUCED IN SWINE

by

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INTRODUCTION

Arthritis is responsible for a serious economic loss to the swine industry. It has been estimated that during the 10-year period from 1942 to 1951 carcass condemnation due to arthritis alone amounted to 24 million dollars annually in the United States (72). This does not include the loss from reduction in rate of gain and feed efficiency.

Mycoplasma hyorhinis, one of the etiological agents of swine arthritis, was recognized by Switzer in 1953 (68). He identified an agent from the nasal cavity of swine that would produce an acute arthritis following an intraperitoneal inoculation. The relative prevalence of M. hyorhinis in swine has been determined by Switzer* (67) and L'Ecuyer et al., (36). Switzer in 1955 (67) reported isolation of this organism from 64 of 96 (66.7%) swine turbinate specimens that exhibited gross turbinate atrophy and 52 of 90 (57.8%) swine turbinate specimens that were apparently normal. L'Ecuyer et al., (36) in 1960 reported the isolation of M. hyorhinis from 51 percent of pneumonic swine lungs that he examined. Switzer in 1961* determined that of 88 arthritic pigs under 125 pounds in weight, 19 (21%) were positive for M. hyorhinis whereas only 1 (0.16%) were positive for Erysipelothrix insidiosa. These

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*Switzer, W. P., Ames, Iowa. Studies on the infectious arthritides of swine. Unpublished data. 1961.

surveys emphasize the prevalence of <u>M. hyorhinis</u> in swine and its importance as an etiological agent of arthritis.

It is imperative that the pathogenesis of the tissue changes caused by this common swine pathogen be known so that a better understanding of this condition might be possible. There are contradictions in the literature as to the histopathological changes of the swine arthritic joints caused by <u>M. hyorhinis</u>. A description of changes in the osseous tissue is completely lacking in the literature.

It was, therefore, concluded that a critical study and evaluation of the macroscopic and histopathological changes of the synovial membranes and osseous tissue in swine at various intervals after intraperitoneal inoculation with <u>M. hyorhinis</u> would make a significant contribution to the understanding of the lesions produced by this pathogen. The gross and histo-pathological changes of the brain and visceral organs are also described. Cytological changes of the synovia and clinical observation of infected animals are presented.

LITERATURE REVIEW

Mycoplasma hyorhinis Arthritis

McNutt et al., (42) reported an active agent isolated from the joints of arthritic pigs. They did not identify the causative agent, but available evidence indicates that they were probably dealing with M. hyorhinis. The lameness observed by these workers occurred primarily in younger animals. The synovial membranes were congested and hemorrhagic. There was an increased amount of joint fluid which was thick, turbid and often blood tinged. In older, more chronic cases, the lesions were associated with a thickening of the periarticular connective tissue. Erosions of the articular surface were not present. These workers state that a histopathological study of these joints revealed no significant changes. Three of 4 pigs which were subcutaneously inoculated developed lameness and the active agent was recovered in chicken embryos.

Switzer (70), while investigating the etiological factors of atrophic rhinitis, isolated an agent from swine nasal turbinates by inoculation of chicken embryos. When this organism was inoculated intraperitoneally into pigs 6 weeks of age, they developed arthritis. He cultivated and characterized this organism and proposed the name Mycoplasma hyorhinis for this arthritis producing agent. Switzer (69) states that 5 to 20 percent of M. hyorhinis inoculated swine will develop arthritis.

Willigan (74) and Willigan and Beamer (75) reported
isolation of a transmissible agent from a pericarditis of
swine that, when inoculated into swine, produced arthritis.
At 1 to 2 weeks postinoculation some of the animals showed
stiffness and pain, especially in the hind legs. Excessive
arching of the back was evident. One pig evidenced erosions
of the metatarsophalangeal articular surface. These erosions
were shallow in depth and irregular in shape. A chronic
periarthritis was evident.

O'Donoghue et al., (48) reported that in a field outbreak
of acute arthritis, probably due to M. hyorhinis, the first
clinical indications of swelling and puffiness of the joint
appeared at 10 days of age. At 8 weeks of age varying numbers
of pigs demonstrated involvement of the joints. Heavy pigs
occasionally developed sudden lameness. Incision of affected
joints disclosed an excessive amount of straw colored fluid.
The results of a histopathological examination of joint tissues
were variable and inconclusive.

Groth (25) stated that polyarthritis produced by M.
hyorhinis may be associated with other visceral lesions, but
occasionally it is the only lesion observed. He stated that
usually a small number of animals in the herd are affected.
Groth observed that the articular cartilages were not affected,
the joint fluid was increased and little, if any, inflammation
of the periarticular tissues was present.

McNutt (41) reported that in field outbreaks of M.

hyorhinis arthritis 10 percent of the young swine may be affected. Any articulation can be involved although the most frequently involved sites are the large, freely moveable joints of either the fore or hind legs. Joint enlargement was accompanied by cloudy, serous to serosanguineous exudate in the joint cavity as well as edema and fibrous proliferations of the periarticular tissues. McNutt (41) stated that the arthritis was continuous, without remissions or exacerbations. Proliferative changes and hyperemia occurred in the synovial membrane. The villi were red and often papilla-like. The inflammatory cells, which were few in number, were mononuclears and usually perivascular in location. He stated that infection does not result in polymorphonuclear leukocytic infiltration of the synovial membrane unless necrosis occurs. The articular cartilages remained normal.

Lecce (34) and Lecce et al., (35) reported an outbreak involving a dual infection of M. hyorhinis and Hemophilus influenzae suis. M. hyorhinis was believed responsible for the inflammatory changes of the synovial membrane.

Arthritis in Glässer's Disease

The lesions produced by Glässer's disease, which affects pigs in Europe and Australia, closely resembles the lesions produced by M. hyorhinis. However, Glässer's disease is commonly associated with Hemophilus influenzae suis. At this time the two diseases are separated because they appear to be

caused by two different etiological agents.

Glässer (21) and Glässer et al., (22) described a fibrin-ous inflammation of the joints of pigs. They were most susceptible to this condition during the first 3 months of life. Shipment and rough handling by the attendant were regarded as predisposing factors. Affected joints were swollen and the skin covering the joint evidenced signs of inflammation. The synovial membranes of affected joints were hyperemic and had an increased amount of a yellowish clouded synovia. Fibrin-ous masses were frequently observed in the joints, either lying loose on the synovial membrane or suspended in the synovia.

Shanks (57) isolated a Gram-negative, hemophilic bacteri-um from swine 10 to 14 weeks of age afflicted with acute ar-thritis. The mortality rate was 75 percent or higher. The joint changes were characterized by a swelling in the joint region. There was an increased amount of synovia with a yellowish-grey material in the joint which was fibrinous in consistency.

Hutyra et al., (29) stated that symptoms of Glässer's disease consisted of lameness, swelling and pain in the affected joints. Postmortem examination revealed a fibrinous deposit on the synovial membrane and a yellow, turbid synovial fluid.

Hjärre and Wramby (27) noted that Glässer's disease occurred in pigs less than 3 to 4 months of age. The

condition may strike within 2 to 3 weeks after transportation. An acute fibrino-purulent arthritis with a turbid synovial fluid was present.

Sutherland and Simmons (66) described several outbreaks of Glässer's disease which were characterized by acute pain in the limbs and joints with death following within 24 to 48 hours. All of the joints were acutely inflamed and contained considerable turbid fluid with light brown flakes which were composed of cells and fibrin. There were fibrinous deposits and small erosions on some of the articular surfaces.

Other Lesions Produced by Mycoplasma hyorhinis

McNutt et al., (42) stated that at 6 days postinoculation there was exudate over the large intestine and omentum in the form of light cream colored strands and flat irregular pieces. Switzer (71) found that if pigs 6 weeks of age or younger were intraperitoneally inoculated with cultures of M. hyorhinis, a severe fibrinous peritonitis developed. Williligan (74) and Williligan and Beamer (75) reported that a non-adherent exudate on the parietal surface of the liver and lungs was produced when pigs were infected with M. hyorhinis. Groth (25) stated that pleuritis, pericarditis and peritonitis were usually associated with a polyarthritis due to M. hyorhinis.

Switzer (69, 70, 71), Williligan (74), Williligan and Beamer (75), Carter and Schroeder (4), O'Donoghue et al., (48) and Groth (25) reported that a pericarditis was usually associated

with M. hyorhinis infection. Switzer (69) and O'Donoghue et al., (48) stated that pericarditis was the most constant lesion.

Switzer (69) stated that histological examination of turbinates from pigs which were intranasally inoculated with M. hyorhinis revealed an increase in lymphocytes, lymphoblasts and macrophages in the submucosal tissue. The lymph follicles present in the submucosa of the nasal turbinates were hyperplastic. Gross turbinate atrophy was not produced by M. hyorhinis.

Carter and Schroeder (4) found that a large percentage of pigs under 2 months of age with pneumonia had pericarditis, pleuritis and peritonitis. A histopathological study of the lungs, from which M. hyorhinis was recovered, revealed changes similar to those described by Hjarre in 1952 for enzootic pneumonia and closely resembled changes seen in virus pneumonia of pigs. Intranasal inoculation with M. hyorhinis alone would not produce pneumonia. However, Runnells et al., (53) state that M. hyorhinis alone causes a serositis, alveolar cell proliferation and a lymphocytic infiltration of the pleura. They state that pneumonic lesions associated with M. hyorhinis resemble an inhalation type bronchial pneumonia. Switzer (70) states that pneumonia could not be produced by intranasal or intraperitoneal inoculation of this organism.

Other Lesions Associated with Glässer's Disease

Glässer (21) reported that in Europe prior to 1910 there frequently occurred a fibrinous inflammation of the serous membranes of swine. This was attributed to Pasteurella multocida infection. In 1910 Glässer observed that the serositis was caused by a small, Gram-negative rod, later identified by Hjärre in 1942 as Hemophilus influenzae suis.

Shanks (57) noted that the disease syndrome described by Glässer was frequently associated with a fibrinous pleuritis, peritonitis and pericarditis.

Hjärre and Wramby (27) and Mayerhofer (40) reported that in addition to the polyserositis, an acute meningitis or meningoencephalitis often occurs in the Glässer's disease syndrome. Less severe cases revealed only a hyperemia of the meninges. In severe cases there were diffuse, yellowish, fibrinous, exudative masses under the dura. In severe cases there was also a marked fibrinopurulent leptomeningitis. An abundance of polymorphonuclear leukocytes and lymphocytes were embedded in a fibrinous network.

Lecce (34) and Lecce et al., (35) reported that a field outbreak of Hemophilus influenzae suis infection in swine produced gross meningeal congestion. Microscopically, the leptomeninges of the cerebrum, cerebellum and brain stem were densely infiltrated with neutrophiles and some macrophages. This infiltration was patchy in some areas and diffuse in

others.   In the cerebral cortex, there was a relative loss of neurons with focal demyelination.   Hemophilus influenzae suis was isolated from the brain.

Swine Erysipelas Arthritis

Ward (73) was the first worker in this country to isolate Erysipeolothrix insidiosa from swine arthritic joints.   Isolations were most frequently made from cases exhibiting distention of the synovial capsule by a serous fluid containing masses or flakes of exudate.   Isolations were less frequent when lesions of the articular cartilages were observed and when numerous large synovial villi and extensive proliferation of periarticular connective tissue were present.   In the blood tinged synovia the lymphocyte was the most common cell.   In joints exhibiting more advanced lesions such as excessive exostosis with ankylosis, the synovial fluid was normal in appearance and generally sterile.

Parker et al., (50) referred to an acute stage of swine erysipelas polyarthritis in which only slight reddening of the synovial villi, with slight periarticular fibrosis, was present.

Ducksbury (15) reported that many cases of arthritis were not detected in the routine antemortem inspection, but that the affected carcasses could be recognized by examination of the iliac and inferior cervical lymph nodes since these glands were swollen 4 to 5 times their normal size, congested and

edematous. The internal iliac gland proved to be a reliable indicator of an arthritis in the corresponding femoro-tibial or coxo-femoral joint. In the affected joints the synovial fluid was increased, blood tinged and turbid. The synovial membrane was swollen and showed numerous marginal hemorrhages.

Collins and Goldie (8) reported that the early lesions of experimental E. insidiosa polyarthritis consisted of edema, congestion, synovial cell proliferation and a slight mononuclear cell infiltration of the synovial membrane. As the arthritis progressed, the edema became less pronounced, cellular proliferation increased, synovial villi increased in size and an increased number of lymphocytes and plasma cells were observed. Minute areas of suppuration were noted in the synovial membrane. Ulceration of the villi occurred. The ulcers were replaced with granulation tissue under a fibrinous exudate containing many polymorphonuclear leukocytes and erythrocytes. The synovia was nonpurulent and contained polymorphonuclear leukocytes, lymphocytes, monocytes, macrophages and synovial lining cells. The percent of neutrophiles in the cells infiltrating the synovia was rarely in excess of 50 percent. The total cell counts were never high. Subchondral fibrosis of the bone marrow and increased vascularity were present. Collins and Goldie (8) stated that pannus formation and superficial erosions of the cartilage at the site of pannus attachment were present. Later stages sometimes showed intra-articular and joint capsule fibrosis.

Grey et al., (24) suggested that arthritis may result from either acute or subclinical erysipelas. They reported that in the early stages of swine erysipelas arthritis, a slight inflammation of the synovial membranes was present. As the lesion becomes chronic, connective tissue proliferation gives rise to synovial fringes, either attached to the synovial membrane or freely suspended in the joint fluid. Osteitis and periosteitis were observed.

Doyle (12, 13) noted that soreness or stiffness was evident in acute cases of erysipelas arthritis. This suggested that a myostitis was present. In chronic cases affecting the carpal joint, the enlargement was usually symmetrical giving that portion of the leg a spindle-shaped appearance. He observed that the tarsal joint often shows a greater enlargement medially than it does laterally. Both proliferative and degenerative changes were noted to occur in arthritic joints. The proliferative changes resulted in increased connective tissue around the joints and hypertrophy and hyperplasia of the synovial villi. The hypertrophied and hyperemic villi sometimes formed reddish, plush-like masses within the joint capsule. Occasionally, a velvet-like membrane extended over a part of the articular surface. Degenerative changes occurred in the articular cartilage and adjacent bone. The articular surfaces were frequently pitted and distorted.

Hughes (28) reported that arthritis was experimentally induced in 16 of 16 pigs given repeated intravenous injections

of Erysipelothrix insidiosa. The joints most frequently
affected were the humero-radial, coxo-femoral, tarsal, femoro-
tibial and carpal joints, in that order.

Sikes (60, 61) and Sikes et al., (62, 63, 64) described
erysipelas arthritis in swine. In animals which survived the
acute form of swine erysipelas, there were usually symptoms
which suggested muscular soreness and tender feet or legs.
Definite symptoms of arthritis occurred later. These workers
noted that acute arthritis developed 2 to 3 weeks postexposure.
Joint effusions distended the capsule and the animals were
very lame and frequently shifted their weight from leg to leg.
The swollen joints were not painful or sensitive to the touch.
Sikes et al., (62) noted that a marked periostitis, ostitis
and, in severe cases, osteomyelitis were present. In the
acute stage of arthritis, the principal changes were charac-
terized by vascular engorgement of the joint capsule and
synovial tissues. The joint effusions were turbid, serosan-
guineous or mucinous. The synovial villi showed beginning
proliferation, extensive vasodilation and initial lymphocytic
infiltration. Sikes et al., (62) noted that by 2 months post-
inoculation a proliferation of the cells covering the hyper-
trophied synovial villi was present. The villi contained
young, highly vascular connective tissue and were infiltrated
by plasma cells and lymphocytes. A striking feature was the
dense collection of lymphocytes in the synovial villi. Sikes
et al., (63) stated that the villi of joints affected with

erysipelas arthritis of 6 months or longer duration frequently resembled granulomatous polyps. In advanced chronic arthritis with pannus formation of subchondral origin there was marked fibrosis, increased vascularity and an infiltration of lymphocytes in the adjacent marrow spaces. In those cases in which the pannus apparently originated from the synovial membrane, subchondral fibrosis was less likely to occur. Pannus attachment to the articular cartilage was accompanied by erosions and destruction of the cartilage.

Sikes (59) compared erysipelas arthritis in swine to rheumatoid arthritis in man. He stated that the synovia is serosanguineous and mucinous, similar to that observed in rheumatoid arthritis. The formation of hypertrophied synovial fringes whose villi become bulbous with focal collections of lymphocytes resembling germinal centers are common to both conditions. In addition, intraarticular fibrous adhesions and rarefaction of bone are common to both conditions.

Neher et al., (47) reported that vaccination of swine against swine erysipelas did not prevent the development of arthritis since a higher incidence of arthritis consistently resulted in the vaccinated pigs when they were exposed to the disease. Of the 50 vaccinated animals which were inoculated intravenously with virulent Erysipelothrix insidiosa, 31 (62%) developed arthritis 2 months after challenge, whereas 1 (14%) of 7 surviving unvaccinated pigs developed chronic arthritis. Sensitization may have been an important etiological factor in

arthritis since marked anaphylactic reactions were evident in the vaccinated swine at the time of injection.

Neher and Swenson (46) reported that erysipelas-like joint lesions could be produced in hypersensitized swine by intraarticular injection of heat-killed cultures of Erysipelo-thrix insidiosa.

Pyogenic Arthritis of Swine

Ward (73) reported that Bacterium pyogenes (Corynebacte-rium pyogenes) was isolated from 1 case of swine polyarthritis. The pathological condition of the case differed from others which were studied in that periarticular abscesses were present. Pigs inoculated intravenously with B. pyogenes developed suppurative lesions in the bones. The lesions in the legs were usually located at the junction of the epiphysis with the shaft. The synovial cavities of adjoining joints contained suppurative exudate and were connected with the bone lesions by a fistulae.

Collier (6) reported that Streptococcus equisimilus was frequently associated with a wide variety of lesions in swine. The joints appeared to be a common site for localization of this organism. Ten of 13 beta hemolytic streptococci isolated from arthritic lesions were S. equisimilus.

Field et al., (17) reported that streptococcal arthritis characterized by a suppurative arthritis is a specific clinical entity occurring in pigs between 2 and 6 weeks of age. He

stated that infection may be confined to a single litter whereas in some herds the disease may appear in successive litters over a period of many months. The streptococci which were isolated did not correspond to any of the Lancefield groups.

Groth (25) reported that streptococcic arthritis affects pigs before weaning age. This type of arthritis is character- ized by a turbid, purulent exudate in the joint space and inflammation of the surrounding tissues. The exudate contained numerous macrophages. Arthritis caused by this organism may persist for a long period of time in pigs that survive the septicemia.

Nutritional Arthritis

Calcium deficiency

Kernkamp (31, 32) reported that 50 percent of the pigs which were fed a ration of 94 parts corn, 5 parts casein and 1 part sodium chloride developed lameness. The gross changes involved the osseous structures of the epiphysis of the long bones. Other changes exhibited were periosteal and subperios- teal hypertrophied areas. Ulceration, erosion and atrophy of the articular cartilages frequently occurred. The most fre- quently involved bones were the humerus, femur, scapula, radius and ulna. These changes could be noted on gross examination but were not commensurate with the clinical manifestations. The spongy bone was soft and the marrow substance was usually

white and of a fatty consistency. Hemorrhage in the extremi-
ties of the long bone shafts and in the epiphysis was observed.
These changes most frequently occurred in the proximal extremi-
ty of the humerus and the distal extremity of the femur. The
subperiosteal hypertrophied areas appeared greyish-white in
color and crumbled easily. Often the thickened periosteal
lesion was situated at a point where it gave additional sup-
port or where there was considerable muscle tension on the
bone. Kernkamp (31) observed that the subperiosteal thicken-
ings were composed of osteoid tissue. Kernkamp (32) stated
that the articular cartilages were contracted and thrown into
wrinkles which caused deep linear furrows. Erosive lesions of
the articular cartilages were sometimes found, especially in
the glenoid cavity of the scapula. In some instances the
cartilage was softer than normal. The synovial membrane was
thickened and in some cases numerous hypertrophied villi were
observed. The trabeculae were usually wide and were not ar-
ranged in a uniform manner. The spaces between the osteoid
thickenings were filled with fine connective tissue fibers as
well as a few osteoblasts, osteoclasts, leukocytes and erythro-
cytes. The connective tissue fibers were arranged in a dense
reticulum. In some cases the inner layer of the periosteum
showed a marked increase in white fibrous connective tissue
fibers. The epiphyseal cartilage was often wide and irregular
and the periphery of the bone was thickened, becoming narrower
toward the center of the bone. The cartilage cells were

arranged in columns separated by varying amounts of hyaline matrix.

Vitamin D deficiency

Golding et al., (23) reported that rickets could not be induced in pigs with various diet combinations of vitamin A and calcium. Although defective calcification was found in the zone of provisional calcification when the diet was deficient in both calcium and vitamin A, no increase in the amount of osteoid tissue occurred. Sunlight was not excluded in this trial.

Zilva et al., (77) stated that rickets was produced in 8 of 10 swine when only sunlight was excluded. The zone of provisional calcification was uneven and lime salt deposits were deficient. In the trabeculae of the primary spongiosa, islands of cartilage cells were present. The trabeculae were curved, interlaced and consisted of osteoid tissue.

Park (49) stated that an excessive amount of osteoid tissue was the cardinal sign of rickets in human beings. This may be the only sign of disease in osteomalacia and in rickets in older children. He stated that the earliest manifestation of rickets was the failure of lime salt deposition in the layer of cartilage next to the shaft. Circulation at the cartilage-shaft border becomes disarranged, thus, orderly endothelial invasion of the cartilage stops. Blood vessels penetrated areas where calcification of the proliferative

zone of the cartilage was defective.

Groth (26), in a comparative histopathological study of rickets and osteodystrophy, stated that 48 swine showed an osteopathy as evidenced by increased pliability of the rib shaft and enlargement of the distal epiphysis of the rib. Examination revealed a widening of the zone of columns and of the vesicular zone of the cartilage as well as suppressed cartilage breakdown. There were thin, distorted trabeculae in the primary spongiosa which contained necrotic and uncalcified cartilage. There were aplasia and hypoplasia of the osteo-blasts. The histological lesions did not resemble those described for rickets. No excessive amount of osteoid tissue was present and the cartilage lacked vascular brushes. Thus, Groth (26) concluded that rickets was not common in swine.

Runnells et al., (53) state that vitamin D deficiency produces a gross enlargement of the costochondral junction. Microscopically, there are numerous capillary buds and endo-thelial cells invading the lacunae of the epiphyseal plate, numerous osteoblasts on the walls of the cartilaginous lacunae and on the osseous and cartilaginous trabeculae and an abun-dance of uncalcified osteoid tissue. They state that although osteoblasts derived from the periosteum produce osteoid tissue at a normal rate, the osteoid tissue does not become properly ossified.

Vitamin A deficiency

Shipley et al., (58) studied the bone changes in guinea pigs that were fed a diet low in vitamin A and found that the epiphyseal cartilage was narrow and that the columns of cartilage cells were short. Calcification of the proliferative zone in contact with the marrow cavity was complete. Each epiphyseal cartilage cell of the zone of mature cartilage was completely enveloped by calcium deposits. They found that few trabeculae were present immediately adjacent to the cartilage. Those trabeculae present were most numerous at the periphery of the bone and were thin. The trabeculae were invested with a layer of fibrous tissue and at the periphery of the trabeculae countless numbers of large mononuclear cells were conspicuous because of the presence of basophilic granulations. The osteoblasts were large and appeared unusually close together. Many of the trabeculae were covered with large numbers of osteoblasts.

Wolbach and Bessey (76) studied bone changes in guinea pigs and reported that vitamin A had a nonspecific affect on endochondral bone formation. The changes resembled those in a bone which had stopped growing due to a lack of calories.

Runnells et al., (53) reported that vitamin A is vitally concerned with the metabolism of the endothelial cells. A deficiency of this vitamin prevents proliferation of endothelial cells of the capillaries and capillary endothelial cells are not converted into ostoblasts. The capillaries in contact

with the cartilage do not accomplish decalcification and
solution of the cartilage. These workers postulated that
because of the inability of the capillaries to achieve carti-
lage breakdown, the epiphyseal plate became unusually broad
and had an undulating surface. The broad zone observed in
this area was composed of cartilage instead of osteoid tissue
as is the case with rickets. The bone marrow showed suppres-
sion of hematopoiesis.

Manganese deficiency

Miller et al., (44) first reported the effect of manga-
nese deficiency on the skeletal growth of swine. Thirty of 60
pigs raised on a manganese deficient diet became lame when the
animal weighed approximately 150 pounds. The condition was
characterized by pain, enlargement of the tarsal joints,
crooked legs and enlargement of the distal ends of the radius
and ulna. They observed that, even though the diet was defi-
cient in manganese, the mineral content of these bones was
within the normal range for swine. The condition was pre-
vented by the addition of 50 to 60 ppm. of manganese to the
diet.

Neher et al., (45) reported that 60 percent of manganese
deficient swine became lame. Shortness of bone length in the
forelegs and hindlegs, a thickening of the bone in the carpal
and tarsal areas and a marked bowing of the front legs oc-
curred. After maturation, the osteodeformities remained

although lameness disappeared. A histological examination revealed a selective retardation of endochondral osteogensis in the growth discs of the radiuses, whereas the ulna continued to grow. Thus, bowed front legs occurred. Radiographically a detectable, generalized rarefaction of bone occurred and areas of complete aplasia were observed in the distal diaphysis of the ulnas of all deficient animals examined when they were 110 and 125 days of age. At 335 days of age no similar rarefied areas were present. The lesions appeared, histologically, similar to the localized form of osteitis fibrosa and were characterized by replacement of cancellous bone with a dense fibrous tissue which was moderately vascular. Neo-osteoid extensions proximal to the growth discs and adjacent to aplastic lesions were a typical finding. The lipotropic action of manganese was demonstrated by excessive obesity in deficient swine as well as increased deposition of fat in the bone.

Copper deficiency

Follis et al., (19) found that swine fed copper deficient diets developed lameness and deformities of the extremities. Many developed fractures of the long bones. A microscopic examination revealed no abnormalities in the appearance of the epiphyseal or costal cartilages. No change occurred in the deposition of inorganic material in the cartilage matrix. The principal alteration occurred in the metaphyseal regions. The

calcified cartilage trabeculae were devoid of osteoid tissue or encasing bone. This condition developed upon cessation of the osteoblastic activity. Spindle shaped cells were present but they did not appear to be functionally active in the sense that osteoid tissue was not being produced. The cortex of the long bones was reduced in thickness. Follis et al., (19) stated that there was a complete dissociation between the chondroblastic and the osteoblastic phase in copper deficiency. The chondroblasts continue to proliferate, while osteoblastic activity ceases.

Miscellaneous deficiencies

Cohen (5) reported that short periods of dietary insufficiency can produce significant changes which are manifest primarily in the vesicular zone of the cartilage or zone undergoing cytomorphosis. Arrested growth occurred as the result of longstanding diseases. The microscopic lesions consisted of extreme thinning of all zones. A thin band of osseous matrix was deposited in the lower ends of the mature cell columns, partially sealing off the columns.

Frandsen et al., (20) found that the condition of the cartilage was a critical index of the nutritive status of the organism. Depending upon the severity of the deficient state, retardation of epiphyseal or costal cartilage cell proliferation was found. A disturbance in protein metabolism led to a prompt decrease in the proliferative activity of the cartilage

cells. Frandsen et al., (20) reported that a protein defi-
ciency interfered with osteoblastic activity. This condition
retarded periosteal and endosteal bone formation and produced
an osteoporotic structure.

Mycoplasma Arthritis of Other Animals

Mycoplasma arthritis of rats and mice

Sabin (55) identified a filter-passing, transmissible
agent with neurolytic properties from a toxoplasma infected
mouse brain. One to 10 days after intracerebral inoculation
into mice, characteristic rolling on the long axis of the body
with or without other nervous symptoms developed. Typical
lesions consisted of necrosis and almost complete dissolution
of the caudal pole of the cerebellum. When this organism was
inoculated intravenously into mice, the inflammatory process
was limited to the periarticular connective tissue and syno-
vial membrane with no involvement of the articular cartilage.
This organism later was named Mycoplasma neurolyticum (3).

Sabin (54) reported that arthritis was produced in 100
percent of the experimental mice when 5 cc. of a 24-hour
culture of M. arthritidis were injected intravenously. Swell-
ing of the joint may appear as early as 4 to 5 days postinocu-
lation. The process was progressive and became chronic
leading to ankylosis, especially of the carpal joints. Patho-
logical changes were limited to the joint. Proliferation of
the synovial membrane, capsule and perichondrium of the

articular cartilage occurred. Proliferation of connective tissue and probably endosteum of the epiphyseal marrow occurred directly below the joint capsule.

Findlay et al., (18) reported that in M. arthritidis polyarthritis of rats, the early lesions consisted of infiltration of polymorphonuclear leukocytes and large mononuclear cells around the joint. Pannus formation occurred. Finally, the joint cavity was invaded with resultant destruction of the articular cartilage and absorption and disorganization of the epiphysis. Mycoplasma was isolated in pure culture from such cases of polyarthritis.

Sabin (54) studied the joint changes of experimental proliferative progressive arthritis due to M. arthritidis in mice. The first day of clinical arthritis was associated with exudate in the joint space. This exudate consisted of mononuclear and polymorphonuclear leukocytes and cells that appeared to be desquamated from the synovial membrane and perichondium. The cartilage was destroyed by the fiftieth day and sometimes was completely replaced by cells which appeared to be immature chondroblasts.

Preston (51) studied arthritis in rats caused by M. arthritidis. This organism produced suppurative lesions in other parts of the body. Gross lesions in the joints were evidenced by swelling and edema, followed by suppuration. Most of the inflammatory changes were periarticular with subsequent abcesses involving all structures of the joint. The

cartilage was attacked relatively late and in some cases was not diseased. Ito et al., (30) reported that a polyarthritis of rats due to M. arthritidis was characterized by redness, swelling, suppuration, necrosis and sometimes natural amputation of the limb or more often the digits.

Mycoplasma arthritis of goats

Cordy et al., (11) described a naturally occurring Mycoplasma arthritis in goats in this country. One to 2 days after an initial rise in temperature, stiffness and lameness became apparent, followed by painful swelling of the leg joints. A fibrino-purulent arthritis was present. The articulations were variably enlarged, especially the carpal joints. The synovial fluid was opaque, yellowish and viscid but the amount was only moderately increased. The inner surface of the capsule was reddened, and villous formations were sometimes marked. They found that hyperemia, edema and leukocyte accumulations were present in the subcutis and other periarticular structures. In the peracute cases, hyperemia of the synovial membrane and a slight excess of opaque joint fluid were present. Microscopically, there was hyperemia and edema associated with a mild infiltration of neutrophiles and mononuclear cells in the periarticular tissue. Little fibrin was present on the luminal surface.

Cordy et al., (10) reported that the mycoplasma isolated from goats was pathogenic for swine. Depression, anorexia and

a distinct lameness appeared in pigs inoculated intravenously with this organism. The joint fluid in 3 of the animals was turbid and contained fibrin. The brains of 2 animals were examined microscopically. Both showed leptomeningeal infiltration by neutrophiles and mononuclear cells. One animal also evidenced a few narrow, perivascular accumulations of mononuclear cells around blood vessels near the ventricles.

Cordy (9), in discussing the goat *Mycoplasma* sp., stated that in early cases or in mildly affected joints, the synovial fluid was yellowish and turbid but only moderately increased in volume. The more severe, typical cases have large amounts of fibrin in the altered joint fluid. These masses of exudate were composed of dense fibrin with many disintegrating neutrophiles. Macroscopically, the synovial membrane was velvety and somewhat reddened with only limited villous proliferation. Such membranes were edematous and hyperemic with extensive infiltration of both mononuclear and neutrophilic leukocytes. In the more chronic cases there was proliferation of synovial cells. The fibrosa of the joint capsule showed less involvement. It usually was edematous and contained perivascular accumulations of mononuclear leukocytes. Occasionally, edema, petechiation and leukocytic infiltrations were seen in the periarticular structures such as muscle and tendon. Cordy (9) stated that in many animals the tendon sheaths showed inflammatory processes identical to that of the soft tissues.

Boidin et al., (2) reported the recovery of *Mycoplasma* sp.

and a large virus from ovine pneumonia lesions. The
Mycoplasma sp. did not produce pneumonia but did cause
arthritis in some experimental sheep.

METHODS OF PROCEDURE

Experimental Design

Six groups of 6 pigs each were used. These animals origi-
nated from the disease-controlled herd maintained in isolation
at the Veterinary Medical Research Institute (V.M.R.I.), Ames,
Iowa. This herd has been in existence for 7 years. Repeated
culturing of the respiratory tract in ox heart infusion-turkey
serum medium by the method described by Ross (52) and repeated
gross and microscopic examination of lungs indicate that this
herd is free of respiratory disease or M. hyorhinis. All ani-
mals received 2 ml. of injectable iron dextran* intramuscular-
ly at 3 days of age. The pigs were weaned at 3 weeks of age
and inoculated 2 to 3 days later. Throughout the experiment,
a complete pig feed devoid of antibiotics was self fed.

Six pigs from each of 6 litters were assigned to groups 1
through 6. Necropsies of animals were performed on: group 1
at 4 days postinoculation, group 2 at 6 days, group 3 at 10
days, group 4 at 15 days, group 5 at 30 days and group 6 at 56
days postinoculation. Two of the 6 pigs in each group were
used as uninoculated controls. All inoculated animals were
housed in isolation units whereas the control animals were
housed in a farrowing house one-half mile from the isolation

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*Produced by Armour Veterinary Laboratories, Kankakee,
Illinois.

units.

Source and Preparation of Inoculum

The isolate of M. hyorhinis which was used, was recovered from pooled nasal swabs from 2 baby pigs and 1 sow submitted to the Iowa Veterinary Medical Diagnostic Laboratory, Ames, Iowa. The initial isolation of M. hyorhinis was made by Switzer in the seventy-sixth passage of a serial passage swine kidney cell culture. This isolate had been passaged 20 times in ox heart infusion-turkey serum medium (71) and then pas- saged 8 times in a medium containing one-half percent swine gastric mucin. The isolate reacted at a satisfactory titer to antisera produced from M. hyorhinis isolated from the nasal cavity, lung and pericardium, but not to antisera prepared from some of the swine joint isolates. This isolate was the most cytopathogenic of several tested for their action on pri- mary swine kidney cell culture. An additional reason for the selection of this isolate was that in preliminary trials this isolate produced arthritis in all inoculated pigs.

All cultures were approximately 48-hours old when inocu- lated into experimental pigs. A uniform turbidity was present in the medium. The pigs were inoculated intraperitoneally with 4 ml. of a 48-hour culture.

Clinical Observation

All animals were observed daily for lameness or other deviations from normal appearance. These observations are summarized in Table 1. Daily temperatures were taken using a Cary clinical thermometer.

Procedures of Necropsy

All pigs were euthanized by administration of 5 ml. of somnopentyl* intraperitoneally. After the animal was unconscious, the brachial vessels were incised. At this time a blood sample was collected for the cultural detection of M. hyorhinis.

Samples for culture were routinely collected from the peritoneal cavity, pericardium, blood, left tibio-tarsal articulation, left femoro-tibial articulation and left humero-radial articulation on sterile cotton swabs and cultured for the presence of M. hyorhinis. The cerebrospinal fluid was collected aseptically from groups 1, 2, 4 and 6. The skin and muscle were removed from over the allanto-occipital region and the area was seared. A 5 ml. syringe fitted with an 18-gauge needle was used to collect the fluid. The peritoneal cavity was sampled immediately after the abdominal cavity was opened. The pericardial fluid was collected after a small incision had

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*Produced by Pitman-Moore Company, Indianapolis, Indiana.

been made in the pericardium with a sterile scalpel. All joints were opened with a sterile scalpel after the subcutaneous tissues had been seared.

All specimens were cultured on 5 percent horse-blood agar and in a medium containing 80 percent ox-heart infusion broth, 20 percent turkey serum and one-half percent gastric mucin (52). Two thousand units of penicillin per ml. and sufficient thallous acetate to give a 1:4000 final concentration were added to each tube of medium (67). Both the blood-agar plates and ox heart infusion-turkey serum medium were incubated at 37 degrees centigrade. Growth of M. hyorhinis, as evidenced by a uniform turbidity of the medium, was verified by the presence of cocco-bacillary organisms on Giemsa stained smears.

Smears of the synovial fluid and joint exudate were made from the left tibio-tarsal articulation and from all joints exhibiting lesions. They were air dried, fixed in methyl alcohol and stained with 1:50 solution of Giemsa stain for 60 minutes. A differential leukocyte cell count was made.

Tissues were routinely collected from the liver, spleen, kidney, adrenal gland, testicle, lung, anterior surface of the tibio-tarsal articulation of the tarsal joints, tibial-tarsal bone, proximal end of the tibia, proximal end of the radius, costochondral junction of the fifth rib and synovial membrane and articular surface of each joint exhibiting lesions. All tissues except the brain were fixed for 48 hours in Zenker's fixative. The tissues were washed in running tap water for

24 hours and stored in 70 percent ethyl alcohol until processed.

The brains were fixed in 10 percent neutral formalin for approximately 10 days. The brains were sectioned and tissues were collected from medulla, pons, cerebellum, midbrain, basal ganglia and the frontal, parietal and temporal lobes of the cerebrum. The blocks were stored in 70 percent ethyl alcohol until processed.

Processing of Tissues

After the bone specimens were fixed in Zenker's fixative, they had decalcified sufficiently for trimming. They were further decalcified overnight in a 5 percent nitric acid solution under a vacuum of 20 to 22 inches of mercury. This was accomplished in a vacuum jar evacuated by means of a portable vacuum pump. After 8 hours in the nitric acid, the tissues were transferred to a 5 percent ammonium hydroxide solution and placed under a vacuum of 20 to 22 inches of mercury for 2 hours.* The bone was washed in running tap water for 6 hours and processed using Technicon dehydrant and clearing agent. All soft tissues and bones were processed through 6 two-hour changes in Technicon dehydrant, 1 two-hour change in Technicon clearing agent and 3 one-hour changes in paraffin (melting

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*Eggert, M. J., Ames, Iowa. Decalcification of pathological specimens. Private communication. 1960.

point of 48 degrees centigrade). All tissues were embedded in Altmann's paraffin mixture (1) and were sectioned at 6 microns.

Three different stains were used. All sections were routinely stained with Harris hematoxylin and eosin (39). Slides of the synovial membrane were stained with Giemsa stain (39). The Giemsa stain was used to help detect M. hyorhinis in the tissue. Lillie's allochrome (37) was used to differentiate osteoid from osseous tissue.

RESULTS

Clinical Observation

The experimental pigs were 3-weeks old and well nourished. They remained normal in appearance until the third day post-inoculation. Twenty-four of 24 inoculated pigs exhibited early evidence of infection as manifested by a roughened hair coat on the third day postinoculation. By the fourth day most animals had begun to shift their weight from one leg to another. However, in groups 1 and 2 no definite limping was observed.

Limping in group 3 first appeared on the third day post-inoculation. In 2 animals, numbered 15 and 17, the limping persisted until necropsy, whereas limping in a third animal number 16 was of 4-days duration.

In group 4 marked limping was not noted. A weakness in the posterior extremities of animal 23 of this group was noted 8 days postinoculation and the condition persisted until the time of necropsy. All inoculated animals had become very gaunt by the time of necropsy on the fifteenth day.

In group 5 which were sacrificed 30 days postinoculation, definite limping developed 5 days postinoculation. Frequent abdominal stretching was observed after approximately 6 days. Swelling of both hocks developed about the tenth day in animal 28. The swelling was more evident on the medial side of the hock joint. By the twenty-second day, the tarsal and femoro-

tibial joints of animal 29 were distended. This distention
was soft and of a fluctuating nature with periarticular hyper-
thermia not detectable.

In the animals of group 6, necropsied 56 days postinocu-
lation, definite limping appeared 5 days postinoculation. The
left femoro-tibial joint of animal 34 was swollen on the sixth
day postinoculation. The limping which developed in this pig
persisted throughout the experiment. By the fifteenth day
both carpal and tarsal joints were distended with fluid. On
the thirty-fifth day animal number 34 was unable to arise.
This condition persisted for 3 days and then regressed until
on the fortieth day lameness was very slight. At 52 days
postinoculation, animal 34 was again unable to arise. At this
time the animal was very hypersensitive when tapped on the
back. The animal could not manipulate either fore or hind leg.

Animal 33 developed a transient lameness 9 days postinocu-
lation but by the thirteenth day was walking normally. Twenty-
eight days postinoculation the animal began periodically
lifting the right front leg and by the thirty-third day it did
not touch the foot to the floor. This animal was lame through-
out the remainder of the experiment. Excessive periarticular
fibrosis was not observed in any of the infected animals.

All infected animals in group 6 were retarded in growth
when necropsied 56 days postinoculation. At the time of
necropsy they were about one-half the size of the control
animals. There was considerable atrophy of the musculature

of the limbs.

Temperature Change

The febrile reaction was quite variable. Some animals had an intermittent rise in temperature in some cases up to 106.2 degrees Fahrenheit while other animals had little change. No definite pattern of temperature elevation could be established.

Recovery of M. hyorhinis

The incidence of recovery of M. hyorhinis from the various sites cultured is tabulated in Table 2. The peritoneum and pericardium were the early sites for localization of the organism as noted by the high percentage of recovery from groups 1, 2, 3 and 4. At 30 days postinoculation the percentage recovery from these sites had decreased to 25 percent. Isolation of M. hyorhinis from the blood was variable and after the 15-day group, all blood samples were negative. The organism was isolated quite consistently from joints with lesions. However, in the joints without lesions the percentage of recovery was low, especially after 6 days postinoculation. Isolation of M. hyorhinis from the cerebrospinal fluid was variable. The organism was present in 100 percent (4/4) of group 1, 0 percent (0/4) of group 2, 75 percent (3/4) of group 4 and 25 percent (1/4) of group 6. Unfortunately, the cerebrospinal fluid was not sampled from groups 3 and 5.

Table 1. Lameness pattern of animals inoculated intraperitoneally with _Mycoplasma hyorhinis_

Animal Number	Days Postinoculation																
	1	2	3	4	5	6	7	8	9	10	12	14	16	18	20	22	24
3	-	-	-	-													
4	-	-	-	-													
5	-	-	-	-													
6	-	-	-	-													
9	-	-	-	1ac	1ac												
10	-	-	-	-	1ac												
11	-	-	-	-	1ac												
12	-	-	-	-	-												
15	-	-	2c	2c	3c	3c	4c	3a 4c	3a 4c								
16	-	-	-	2c	2c	3c	2c	-	-								
17	-	-	-	-	-	2a	3a	2d	3a								
18	-	-	-	-	-	-	2c	-	-								
21	-	-	-	-	-	-	-	-	-	-	-	-					

1 - Shifts weight from one leg to another   a - right hind leg
2 - Lameness (slight)   b - right front leg
3 - Lameness (Moderate)   c - left hind leg
4 - Lameness (severe)   d - left front leg

Table 1 (Continued)

Animal Number	Days Postinoculation																
	1	2	3	4	5	6	7	8	9	10	12	14	16	18	20	22	24
22	-	-	-	-	1ac	-	-	-	-	-	2d	2d					
23	-	-	-	-	-	-	-	2a 1c	2a	2a	-	-					
24	-	-	-	1ac	-	-	-	-	-	-	2ac	3ac					
27	-	-	-	-	-	-	-	2a	2c	-	-	-	-	-	-	-	-
28	-	-	1ac	-	2a	2a	2a	2a	2a	3ac	3a 2c	3a 2a	2a 2c	2a 2a	2a 2a	2a 3ac	2a
29	-	-	1ac	-	-	2c	-	-	2c	2c	2ad	3d	4d	3d	3d	4d	4cd
30	-	-	1ac	-	1ac	1ac	2a	2a	2a	2b	-	-	1b	3b	4b	3b	3b
33	-	-	-	-	-	-	-	-	-	2c	1c	-	-	-	-	-	-
34	-	-	-	-	1c	2c 4d	2c 1d	2c	2c	2c	3c	4c*	3c 4a	3a 3c	2a 3c	3ac 3a	3ac
35	-	-	-	-	-	-	-	-	-	1a	3a	4ac	3c	3ac	3ac	2c	2ac
36	-	-	-	-	-	-	-	1ac	2a	1ac	-	-	-	-	-	-	-

*Animal was unable to arise

Table 1 (Continued)

Animal Number	Days Postinoculation													
	28	30	32	34	36	38	40	42	44	46	48	50	52	54
27	-													
28	2a 3c													
29	4d													
30	4b													
33	1b 2a	1b	3b	2a 4b	2ac 4b	2ac 4b	4b 2c	4b 2c	2a 4b	4b	1ac 4b	4b	4b	4b
34	3c	3ac	2ac	1ac 3ac	4ac* 2d 3ac	2d 2ac	2ac 2b	2b	-	1a	1ac	1ac	4ac*	4ac*
35	3ac	4ac	3ac	2b	3b	2b	2ac	2ac	2ac	2ac	2ac	2ac	2ac	2ac
36	-	-	-	-	-	-	-	-	-	-	-	-	-	-

*Animal was unable to arise

Table 2. Isolation of Mycoplasma hyorhinis from pigs inoculated intraperitoneally with this organism

| | Days Postinoculation | | | | | | |
	4 days	6 days	10 days	15 days	30 days	56 days	Controls for all groups
Peritoneum	100%[a](4/4)[b]	75%(3/4)	100%(4/4)	100%(4/4)	25%(1/4)	0%(0/4)	0%(0/12)
Pericardium	100%(4/4)	75%(3/4)	75%(3/4)	100%(4/4)	25%(1/4)	25%(1/4)	0%(0/12)
Blood	25%(1/4)	0%(0/4)	25%(1/4)	50%(2/4)	0%(0/4)	0%(0/4)	0%(0/12)
Joints with lesions	100%(3/3)[c]	50%(2/4)[c]	100%(9/9)	86%(6/7)	90%(10/11)	75%(12/16)	0%(0/12)
Joints without lesions	30%(3/10)	50%(4/8)	16%(2/12)	0%(0/10)	29%(2/7)	0%(0/6)	0%(0/12)
Cerebrospinal fluid	100%(4/4)	0%(0/4)	-[d]	75%(3/4)	-[d]	25%(1/4)	0%(0/12)

a - Percent of animals from which M. hyorhinis was recovered
b - Numerator   - number of pigs from which M. hyorhinis was isolated
   Denominator - number of pigs or joints sampled
c - Lesions were confined to a faint hyperemia of the synovial membranes
d - Not sampled

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Synovial Membrane Lesions

Group 1

The joint changes are tabulated in Table 3. Neither gross nor microscopic lesions of the synovial membranes were found in the animals of group 1 necropsied 4 days postinoculation.

Group 2

A faint hyperemia of the synovial membrane of the right femoro-tibial articulation of animal 9 and the right coxo-femoral articulation of animal 11 was present. The microscopic synovial membrane changes consisted of an increase in the number of neutrophiles and lymphocytes in the blood vessels. No apparent change was present in the blood vessels of the control animals.

Group 3

The synovial membranes of the animals necropsied 10 days postinoculation exhibited marked inflammatory changes. A large mass of fibrin was attached to the synovial membrane of the tibio-tarsal articulation in animal 15 (Figure 2). The membrane under the fibrin was very hyperemic. The synovial membranes of other involved joints were also very hyperemic, especially near the tips of the synovial villi (Figure 3).

Microscopically, the more acutely involved synovial membranes evidenced enlargement of the synovial cells. In the

subsynovial cell spaces an extensive cellular infiltration
that was composed primarily of plasma cells and mononuclear
cells, a few lymphocytes and occasionally neutrophiles was
present (Figure 10). The nuclei of many of these mononuclear
cells were similar to the nuclei of the synovial cells. When
stained with Giemsa stain, there was an occasional degenerated
mononuclear cell with cytoplasmic bodies resembling M. hyo-
rhinis (Figure 14). In areas where fibrin was present on the
luminal surface of the synovial membrane there was an exten-
sive infiltration of neutrophiles in the synovial membrane
(Figure 11). The peroneus tertius tendon sheath of animal 15
was infiltrated with large macrophages. In joints that exhib-
ited mild gross inflammatory changes, the synovial cell layer
was normal and the subsynovial cellular infiltration was com-
posed primarily of plasma cells, macrophages and a few neutro-
philes (Figures 12, 13). Hyperemia of the synovial membrane
was present in such joints.

There was a 2- to 3-fold increase of a clear to slightly
turbid synovial fluid in most affected joints. However, in
animal 15 the synovial fluid was serosanguineous. Large
flakes of fibrin were present in the synovial fluid of some
animals. Microscopically, there was a marked increase in the
number of neutrophiles and the amount of fibrin in the syno-
vial fluid. Eighty percent of the cells in the synovial fluid
in the left carpal joints of animal 15 were neutrophiles.

Group 4

Gross changes in the synovial membrane were minimal in the animals of group 4. Hyperemia of the synovial membranes varied from slight to moderate in all affected joints. Some joints contained a large volume of synovia, even though the synovial membrane was normal in appearance.

The synovial cell nuclei were quite enlarged and resembled those of the cells which were seen in the subsynovial spaces at 10 days postinoculation. In many areas an extensive layer of large nucleated macrophages was present just under the synovial cell layer. Frequently, a marked perivascular lymphocytic cuffing was present. However, lymphocytic foci were not associated with blood vessels in many areas. In the less severely affected joints, the synovial cells were fewer in number and their nuclei were somewhat smaller than the more acutely involved joints. There was a slight increase in lymphocytes and plasma cells in the subsynovial cell layer. Hyperemia of the synovial membrane was minimal in some cases. There was an increase in size of the synovial villi of most of the affected joints in animal 24. There was fibrin formation on the luminal surface with subsequent neutrophilic and mononuclear macrophage infiltration of the subsynovial cell spaces. Fibrous connective tissue formation was present in the center of the hypertrophied villi and around many vessels. Even though the synovial villi of animal 24 were hypertrophied the lymphoid reaction resembled that seen in the more severely

involved joints.

There was a 2- to 4-fold increase in synovial fluid which was turbid and contained large particles of fibrin. The synovial membranes of the control animals remained grossly and microscopically normal. The principal cell type present in the synovia was the neutrophile which comprised 65 to 71 percent of the total number.

Group 5

All infected animals necropsied 30 days postinoculation had gross and microscopic changes of the synovial membranes. The number of joints involved per pig varied from 1 to 5. The synovial membranes were thickened, edematous and velvet-like in appearance. Hyperemia of the synovial membrane varied from marked to mild. In the joints exhibiting minimal hyperemia, there was a variable yellowish coloration of the synovial membrane (Figure 5). The synovial membranes of the control animals remained grossly and microscopically normal (Figures 1, 9).

Enlargement of the synovial villi apparently resulted from hypertrophy and hyperplasia of the synovial cells and the infiltration of inflammatory exudate (Figure 16). A layer of macrophages with large vesicular nuclei was adjacent to the luminal surface of the synovial membrane. Many distinct cell masses consisting of plasma cells and lymphocytes were accentuated by clear zones surrounding them (Figure 15). Many

villi were diffusely infiltrated with lymphocytes whereas in other villi a nodular type of lymphocytic infiltration was present (Figure 16). Increased vascularization of some villi was present. Small foci of fibrinoid necrosis was occasionally present on the luminal surface of the synovial membrane. In such necrotic areas neutrophiles were abundant in the synovial membrane. Pericapsular fibrosis was mild to absent in this group.

The synovial fluid from the involved joints of the animals of group 5 was turbid to serosanguineous and was increased 2- to 5-fold in volume. The predominant cell present in the synovial fluid was the neutrophile. These cells ranged from 33 percent to 74 percent. The synovia of the control animals remained relatively acellular.

Group 6

Gross and microscopic changes were present in the synovial membranes of all infected animals necropsied 56 days after infection, even though animal 36 exhibited only a mild transient lameness at 9 days postinoculation. One to 5 joints were involved per pig. All uninoculated animals remained normal. The affected synovial membranes of the inoculated animals were velvety in appearance and yellowish to pinkish in color (Figure 7). An occasional hyperemic synovial membrane was observed. The right humero-radial joint of animal 33 appeared deficient in synovial fluid. The synovial membrane

was yellow in color and velvet-like in appearance. Slight
periarticular fibrosis was present. A pannus covered the
middle two-thirds of the proximal end of the articular surface
of the radius. This pannus was also attached to the distal
end of the humerus forming a fibrous ankylosis of the joint
(Figure 8). In animal 34 the articular cartilage of the right
coxo-femoral joint was soft and was easily detached from the
subchondral bone (Figure 20). A yellow gelatinous edema was
present around the tendon and perimysium of the peroneus ter-
tius and biceps muscle of animals 34 and 35.

Microscopically, the involved synovial membranes of the
animals in group 6 exhibited hypertrophy of the synovial villi
with connective tissue formation within some villi. Hyper-
plasia of the synovial cells was present (Figure 18). The
nuclei were located in the basal part of the synovial cells.
Lymphocytic perivascular infiltration and lymphoid nodular
formation were present in most villi. Many of the lymphoid
nodules contained germinal like centers with an occasional
mitotic figure (Figure 19). In general, the lymphoid cells
were smaller in size than those noted in the animals of the
30-day sampling. An apparent diminution of lymphocytes in
many lymphocytic foci was occurring since the cells were less
densely arranged than at previous samplings (Figure 17). Neu-
trophiles were present in the subsynovial cell spaces in many
areas. Increased vascularization of the hypertrophied villi
was present. In some mildly affected joints there was little

microscopic change observed in the synovial villi except for occasional foci of lymphocytes and neutrophiles infiltrating the subsynovial cell layer. Only slight pericapsular connective tissue formation was present.

Animals 34 and 36 had a 4- to 5-fold increase in synovial fluid which was mucinous and turbid (Figure 6). Occasionally, flakes of fibrin were present in the synovia. The predominant cell type of the synovia was the neutrophile. The percentage varied from 59 to 79 in the synovial fluids. A small hyperchromatic cell which resembled a degenerating neutrophile was frequently present in the synovia. The synovia of the control animals was relatively acellular.

Table 3. Summary of gross joint lesions in pigs inoculated intraperitoneally with Mycoplasma hyorhinis and in uninoculated control animals

Days Postinoculation	Animal Number	Lesions
4 days	1	No visible lesions (Uninoculated control).
4 days	2	No visible lesions (Uninoculated control).
4 days	3	R. femoro-tibial joint: Mild hyperemia of the synovial membranes. Slight increase in synovial fluid. L. tarsal joints: Mild hyperemia of synovial membranes. No change in synovial fluid. R. scapulo-humeral joint: Mild hyperemia of synovial membrane. No change in synovial fluid.
4 days	4	No visible lesions.
4 days	5	No visible lesions.
4 days	6	No visible lesions.

Table 3 (Continued)

Days Postinocu- lation	Animal Number	Lesions
6 days	7	No visible lesions (Uninoculated control).
6 days	8	No visible lesions (Uninoculated control).
6 days	9	R. femoro-tibial joint: Foci of hyperemia of tips of synovial villi.
6 days	10	No visible lesions.
6 days	11	L. humero-radial joint: Mild hyperemia of synovial membrane. Increase in tenacious synovial fluid.
6 days	12	L. humero-radial joint: Mild hyperemia of synovial membrane. Synovial fluid was tenacious.
10 days	13	No visible lesions (Uninoculated control).
10 days	14	No visible lesions (Uninoculated control).
10 days	15	R. tarsal joints: Synovial membranes are hyperemic and edematous. A large sheet of fibrin was attached to the synovial membrane. Increase of serosanguineous synovial fluid. R. coxo-femoral joint: Synovial membranes are very hyperemic. Increased amount of turbid synovial fluid.
10 days	16	No visible lesions.
10 days	17	L. tarsal joints: hyperemia of synovial membrane. Increase in serosanguineous synovial fluid which contained tags of fibrin. L. coxo-femoral joint: Hyperemia of synovial membrane with increase in clear synovial fluid. R. humero-radial joint: Hyperemia of synovial membrane with increase in clear synovial fluid. R. carpal joints: Hyperemia of synovial membrane especially near the tips of the villi. Synovial fluid normal.
10 days	18	R. humero-radial joint: Petechial hemorrhagic foci on the lateral side of distal end of the humerus just lateral to the condyles. R. tarsal joints: Mild hyperemia of synovial membrane. Increased amount of clear

Table 3 (Continued)

Days Postinoculation	Animal Number	Lesions
10 days	18	synovial fluid.
15 days	19	No visible lesions (Uninoculated control).
15 days	20	No visible lesions (Uninoculated control).
15 days	21	No visible lesions.
15 days	22	L. carpal joints: Little change in synovial membrane. Approximately 2-fold increase in clear synovial fluid.
15 days	23	R. carpal joints. Mild hyperemia of synovial membrane.
15 days	24	L. coxo-femoral joint: Hyperemia of synovial membrane. 3-fold increase of very turbid synovial fluid which contained large flakes of fibrin. L. carpal joints: Hyperemia of synovial membrane. 2-fold increase in turbid synovial fluid. L. tarsal joints: Little change in synovial membrane. 3-fold increase in clear synovial fluid. R. carpal joints: Hyperemia of synovial membrane. 2-fold increase in synovial fluid. R. tarsal joints: Little change in synovial membrane. 4-fold increase in very turbid synovial fluid.
30 days	25	No visible lesions (Uninoculated control).
30 days	26	No visible lesions (Uninoculated control).
30 days	27	L. humero-radial joint: Synovial membrane normal in color but thickened and edematous. 5-fold increase in turbid synovial fluid.
30 days	28	R. coxo-femoral joint: Synovial membranes very hyperemic and edematous. Increase in turbid synovial fluid. L. tarsal joints: Synovial membranes very hyperemic and edematous. Increase in turbid serosanguineous synovial fluid. R. tarsal joints: Synovial membrane not too hyperemic but edematous. Increase in thick synovial fluid.

Table 3 (Continued)

Days Postinocu- lation	Animal Number	Lesions
30 days	29	L. femoro-tibial joint: Pinkish-yellow coloration of synovial membrane which is edematous and thickened. 5-fold increase in turbid synovial fluid. L. tarsal joints: Hyperemia of synovial membrane. Increase in turbid viscid synovial fluid. L. scapulo-humeral joint: Hyperemia of synovial membrane. Increase in sero-sanguineous synovial fluid. R. humero-radial joint: Synovial membrane thickened and edematous but not hyperemic. Increase in turbid viscid synovial fluid. R. carpal joints: Synovial membrane pinkish-yellow coloration and edematous. Increase of turbid viscid synovial fluid.
30 days	30	L. humero-radial joint: Synovial membrane edematous, thickened and slightly hyperemic. 5-fold increase in turbid synovial fluid. R. humero-radial joint: Synovial membrane edematous, thickened and slightly hyperemic. 5-fold increase in turbid synovial fluid.
56 days	31	No visible lesions (Uninoculated control).
56 days	32	No visible lesions (Uninoculated control).
56 days	33	L. tarsal joints: 2-fold increase in clear synovial fluid. R. humero-radial joint: Synovial membrane was pinkish yellow in color and velvety in appearance. Beginning periarticular fibrosis was present. Fibro-hemorrhagic pannus formation which had formed a fibro-ankylosis. The synovial fluid was scant to non-existent.
56 days	34	L. coxo-femoral joint: Mild hyperemia with velvet-like proliferation of synovial membrane. Increase of turbid synovial fluid. R. coxo-femoral joint: Synovial membrane about normal. Necrosis of articular

Table 3 (Continued)

Days Postinoculation	Animal Number	Lesions
56 days	34	cartilage. 3-fold increase in synovial fluid.
		R. and L. carpal joints: Velvet-like proliferation and yellowish coloration of synovial membrane. 4-fold increase in very turbid synovial fluid.
		R. and L. humero-radial joints: Synovial membrane almost normal in color and velvet-like in appearance. 5-fold increase in turbid synovial fluid.
		R. femoro-tibial joint: Synovial membranes were very velvet-like and yellow in color. 10-fold increase of a very stringy turbid synovial fluid. Gelatinous edema around extensor tendons.
56 days	35	R. coxo-femoral joint: A velvet-like proliferation and purplish coloration of synovial membrane were present. Increase in turbid synovial fluid.
		R. and L. tarsal joints: Synovial membrane normal with increase of clear synovial fluid.
		L. femoro-tibial joint: Yellowish coloration and velvet-like proliferation of the synovial membrane. 4-fold increase in synovial fluid. Yellow gelatinous edema around the peroneus tertius tendon.
		R. scapulo-humeral joint: Hyperemia of synovial membrane. 2-fold increase of serosanguineous synovial fluid.
56 days	36	L. scapulo-humeral joint: Hyperemia of synovial membrane. Synovial fluid normal.

Bone Lesions

The only gross bone change noted was in group 6. In these animals the rib shafts evidenced an increased pliability.

Figure 1. A normal synovial membrane of the tibio-tibial tarsal articulation of the tarsal joints from animal 26 (2185). 10 days postinoculation.

Figure 2. The severely involved synovial membrane of the tibio-tibial tarsal articulation is from animal 15 (2162). Note the large sheet of fibrin that was attached to the synovial membrane. Animal 13 (2160) is the uninoculated control animal. 10 days postinoculation.
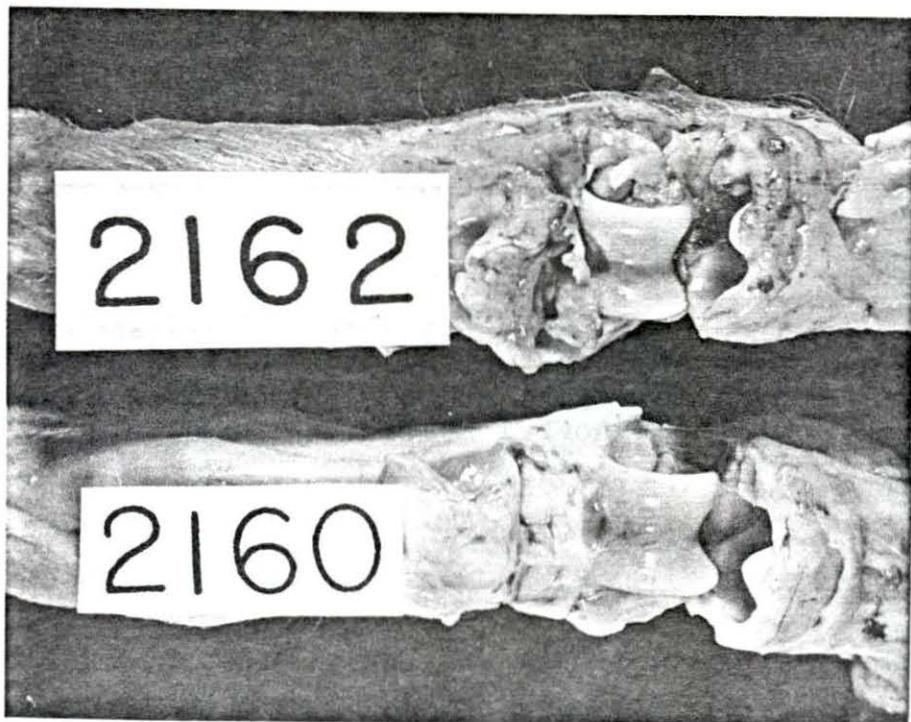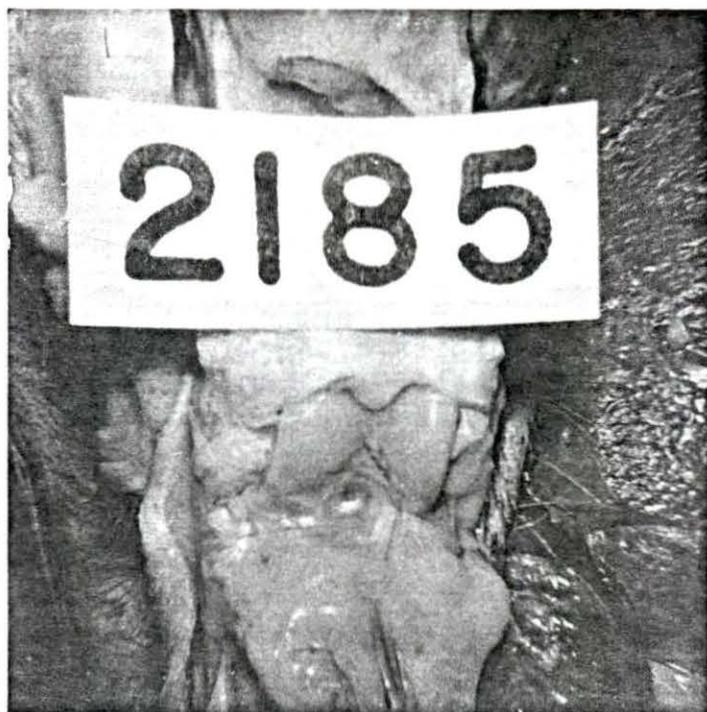
Figure 3. The radio-carpal articulation of animal 15
(2162) exhibits hyperemia of the tips of the
synovial villi. The coxo-femoral joint exhibits
mild hyperemia of the synovial membrane. 10
days postinoculation.

Figure 4. The scapulo-humeral joint of animal 29 exhibits
hyperemia and velvet-like proliferation of the
synovial villi and a slight yellow coloration
of the synovial membrane. 30 days postinocula-
tion.
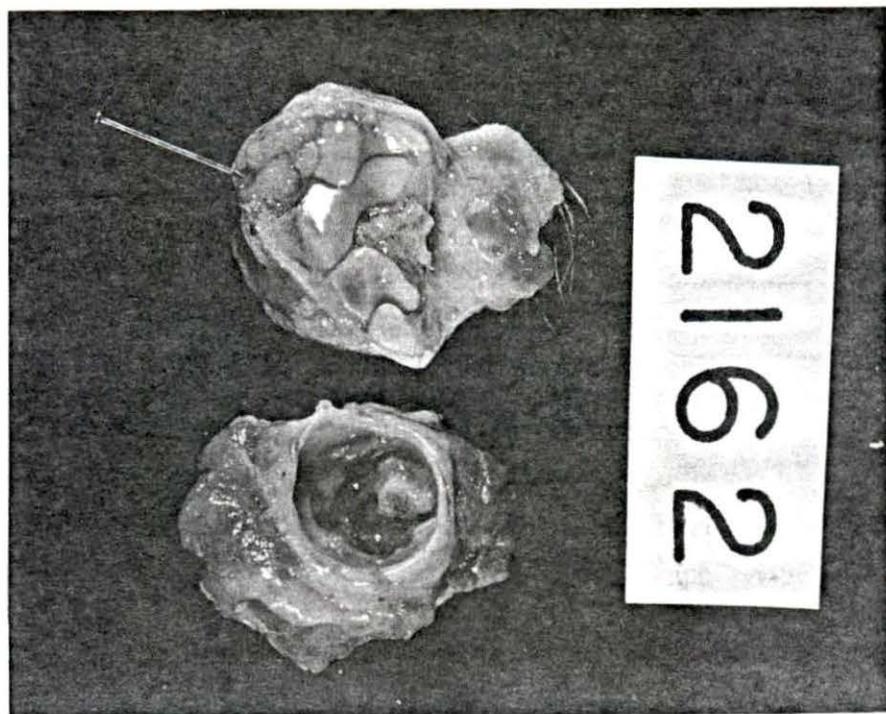
Figure 5. A chronic synovitis of the synovial membrane
           of the femoro-patellar articulation is present
           in animal 29. Note the yellowish coloration of
           the synovial membrane. 30 days postinoculation.

Figure 6. A chronic M. hyorhinis involvement of the
           humero-radial joint in animal 34 is present.
           Note the turbid synovial fluid in this joint.
           56 days postinoculation.
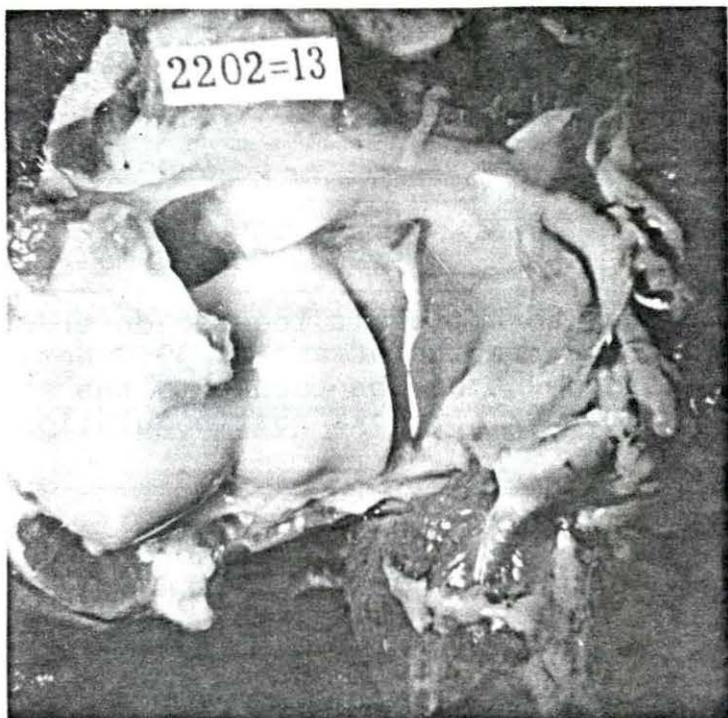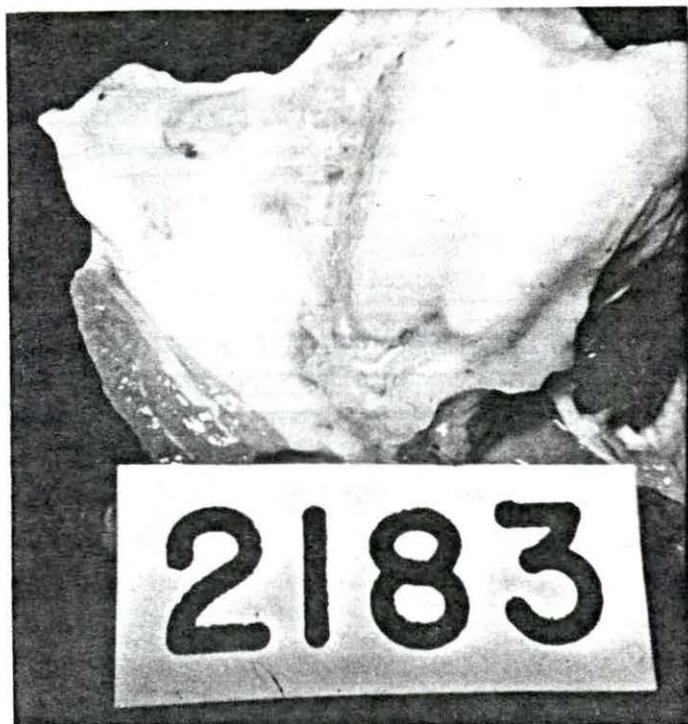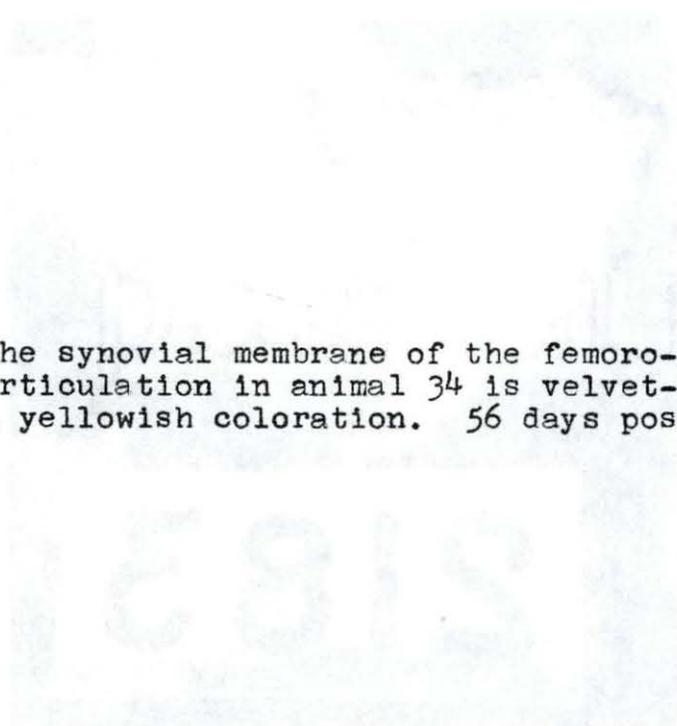
Figure 7.   The synovial membrane of the femoro-patellar
articulation in animal 34 is velvet-like and has
a yellowish coloration.   56 days postinoculation.
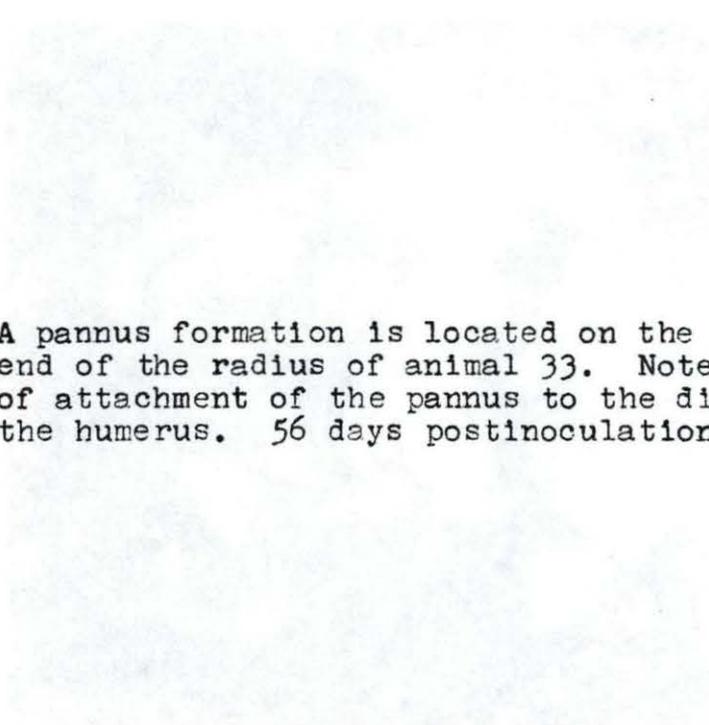
Figure 8.   A pannus formation is located on the proximal
end of the radius of animal 33.   Note the point
of attachment of the pannus to the distal end of
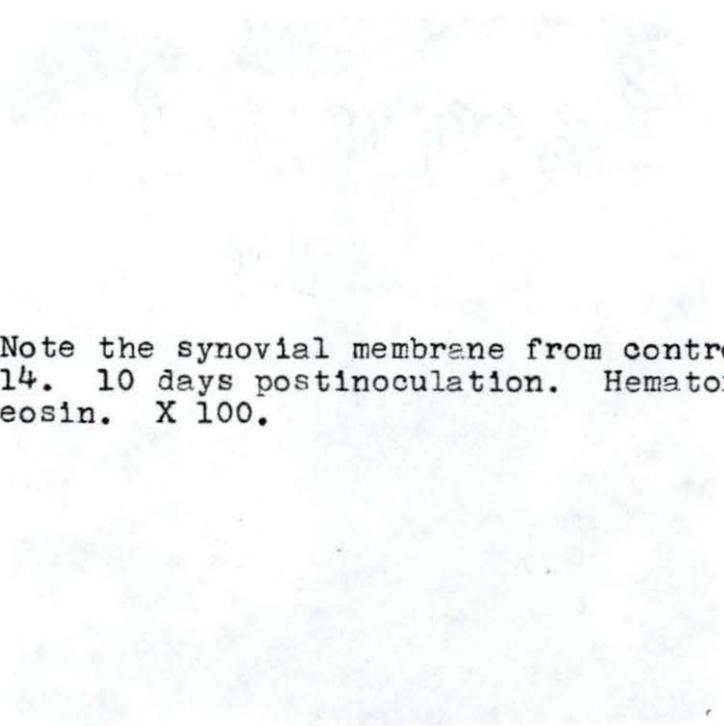the humerus.   56 days postinoculation.
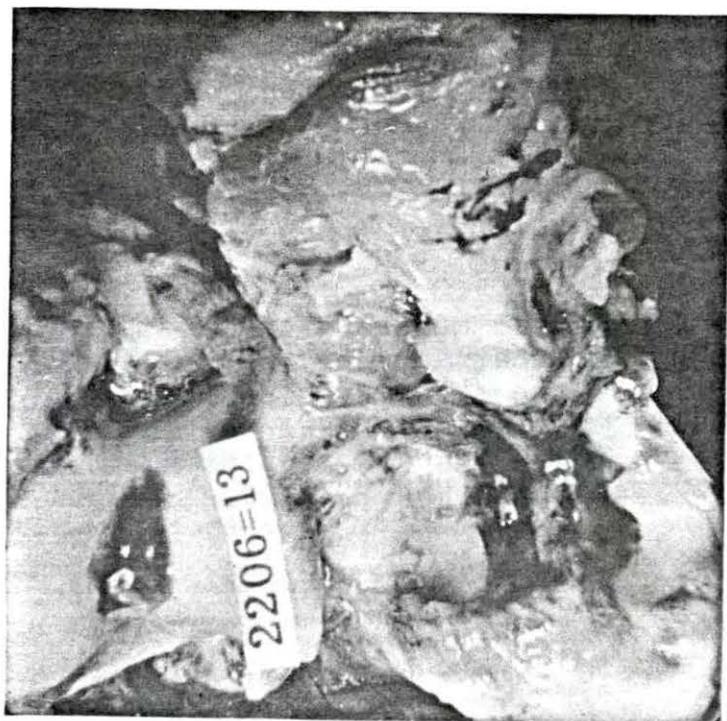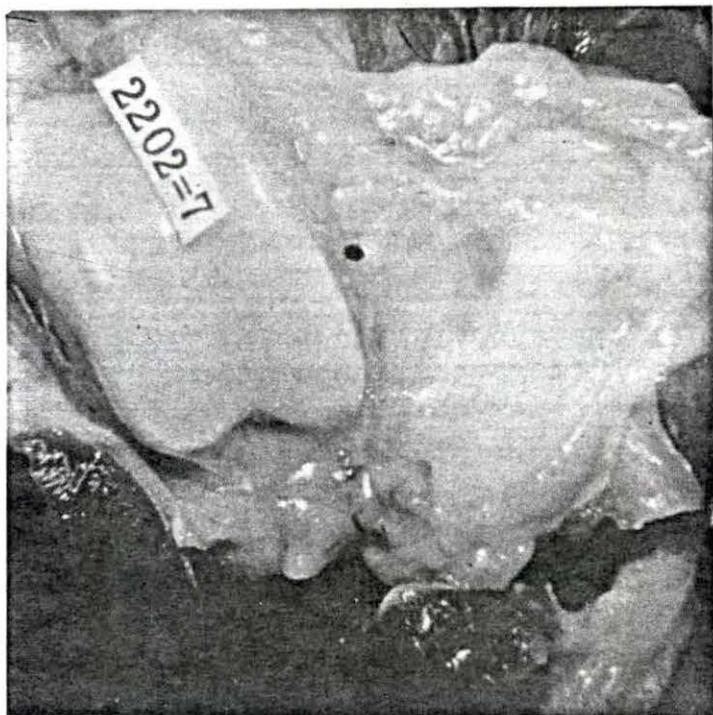
Figure 9. Note the synovial membrane from control animal
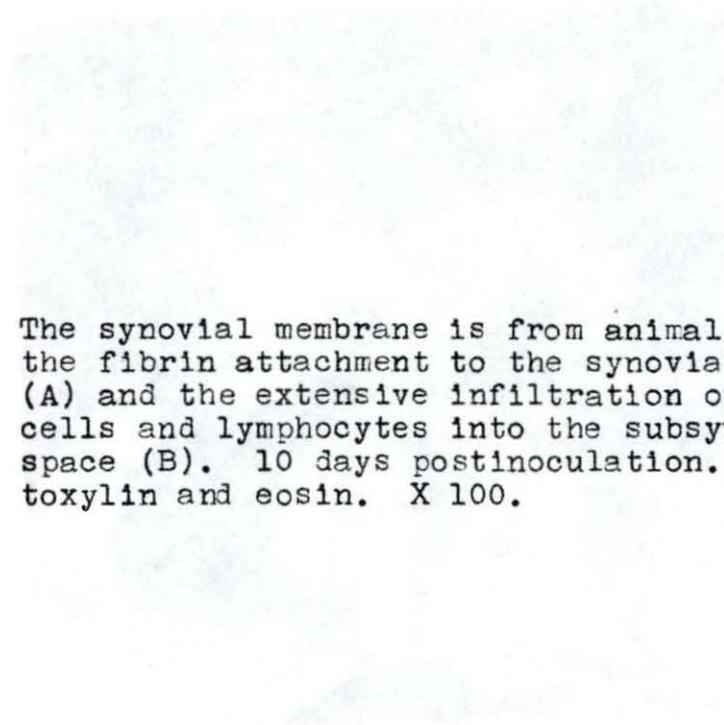   14. 10 days postinoculation. Hematoxylin and
           eosin. X 100.

Figure 10. The synovial membrane is from animal 22. Note
            the fibrin attachment to the synovial membrane
            (A) and the extensive infiltration of plasma
            cells and lymphocytes into the subsynovial cell
            space (B). 10 days postinoculation. Hema-
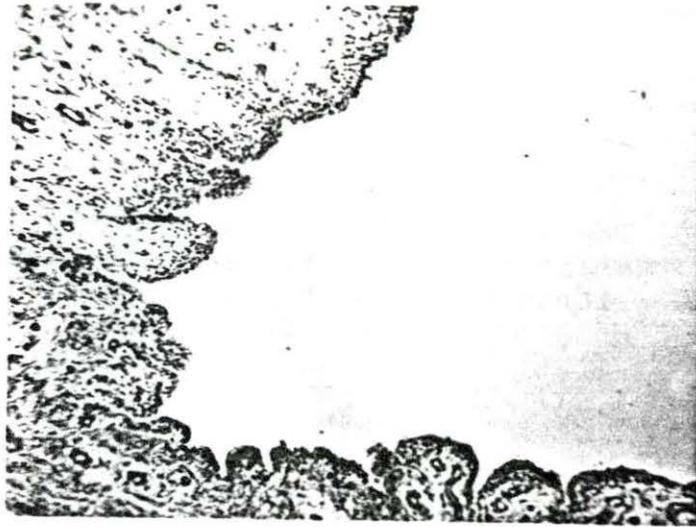   toxylin and eosin. X 100.

Figure 11. The synovial membrane of animal 22 exhibits an
            area of neutrophile infiltration at the point of
            fibrin attachment. 10 days postinoculation.
            Hematoxylin and eosin. X 400.

Figure 12. The synovial membrane of animal 21 exhibits
            mild cellular inflammatory changes. Note the
            cellular infiltration of the subsynovial cell
            spaces. 10 days postinoculation. Hematoxylin
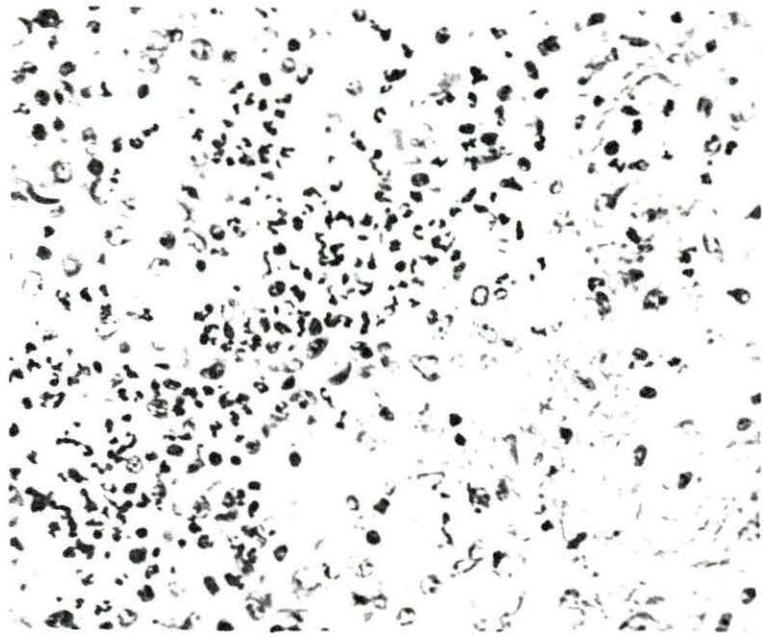   and eosin. X 95.

Figure 13. A more highly magnified view of Figure 12
demonstrates the plasma cell infiltration of
the subsynovial cell spaces. 10 days post-
inoculation. Hematoxylin and eosin. X 400.

Figure 14. The inflammatory exudate of the subsynovial
cell spaces of animal 22. Note the degenerated
mononuclear cell which contains cytoplasmic
bodies resembling M. hyorhinis (A). 10 days
postinoculation. Giemsa stain. X 1500.
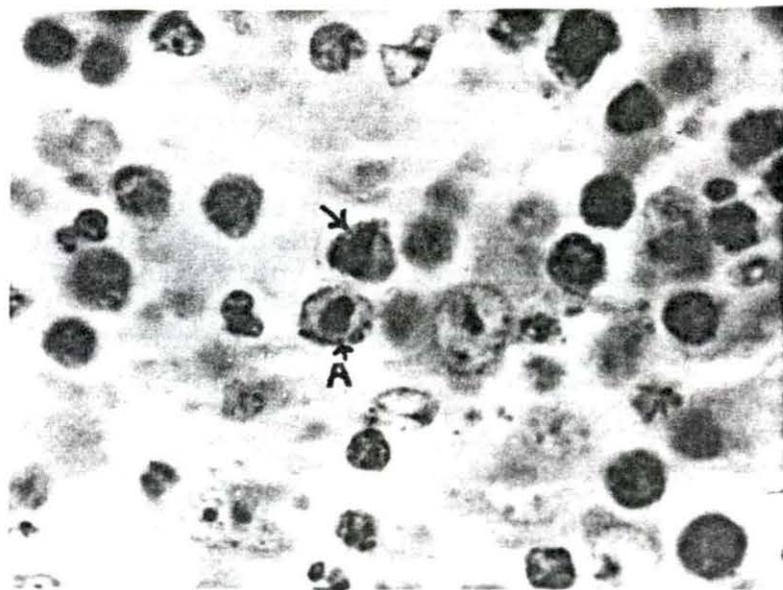
Figure 15.   The synovial membrane inflammatory changes of
              animal 30. Note the clear zones around the
              lymphocyte and plasma cell foci, thus suggestive
              of edema. Also hypertrophy of the villi and
              hyperplasia of the synovial cells are present.
              30 days postinoculation. Hematoxylin and eosin.
              X 95.

Figure 16.   The synovial membrane inflammatory changes of
              animal 27 are present. Note the lymphocyte and
              plasma cell foci within the villi. Also hyper-
              trophy of the villi is present. 30 days post-
              inoculation. Hematoxylin and eosin. X 160.
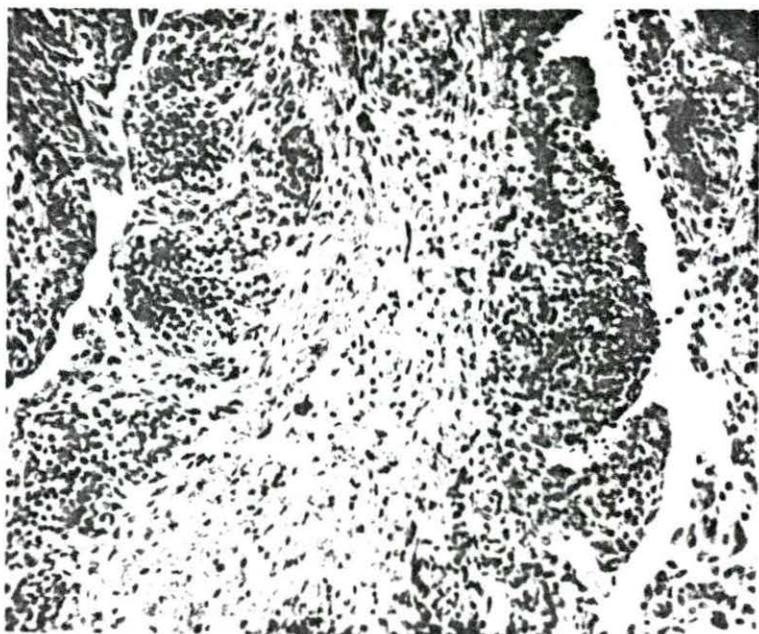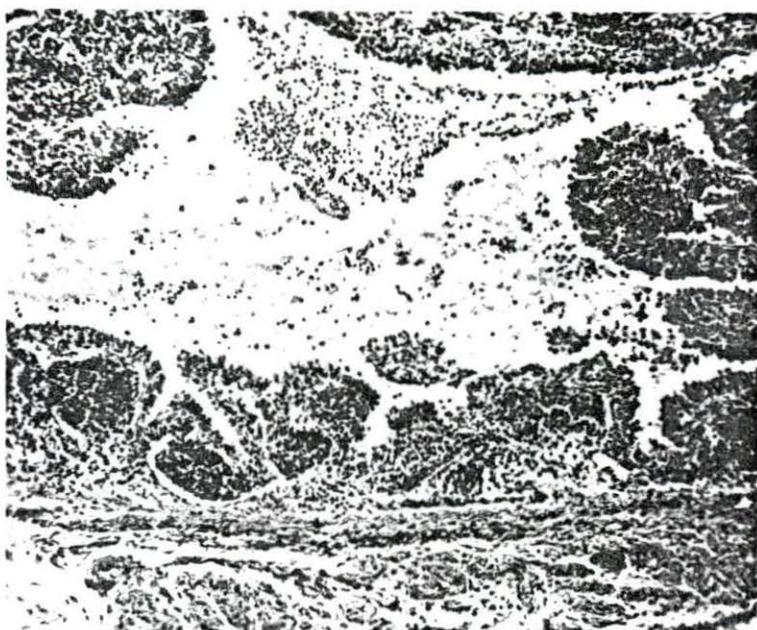
Figure 17.   Hypertrophy of the synovial villi of animal 34
              is present. Note the focal cellular accumula-
              tions consisting primarily of lymphocytes.
              There is a general tendency of lymphocyte
              depletion when compared with the inflammatory
              cellular accumulations at 30 days postinocula-
              tion. 56 days postinoculation. Hematoxylin
              and eosin. X 60.

Figure 18.   Note hypertrophy of the synovial villi and
              hyperplasia of the synovial cells from animal
              34. The inflammatory cell type of the
              synovial membrane is predominantly lymphocytes.
              56 days postinoculation. Hematoxylin and
              eosin. X 160.

Figure 19. A lymphoid nodule containing a germinal-like
center is present in animal 33. Also note the
synovial cells with their nuclei in a basal
position. 56 days postinoculation. Hema-
toxylin and eosin. X 400.
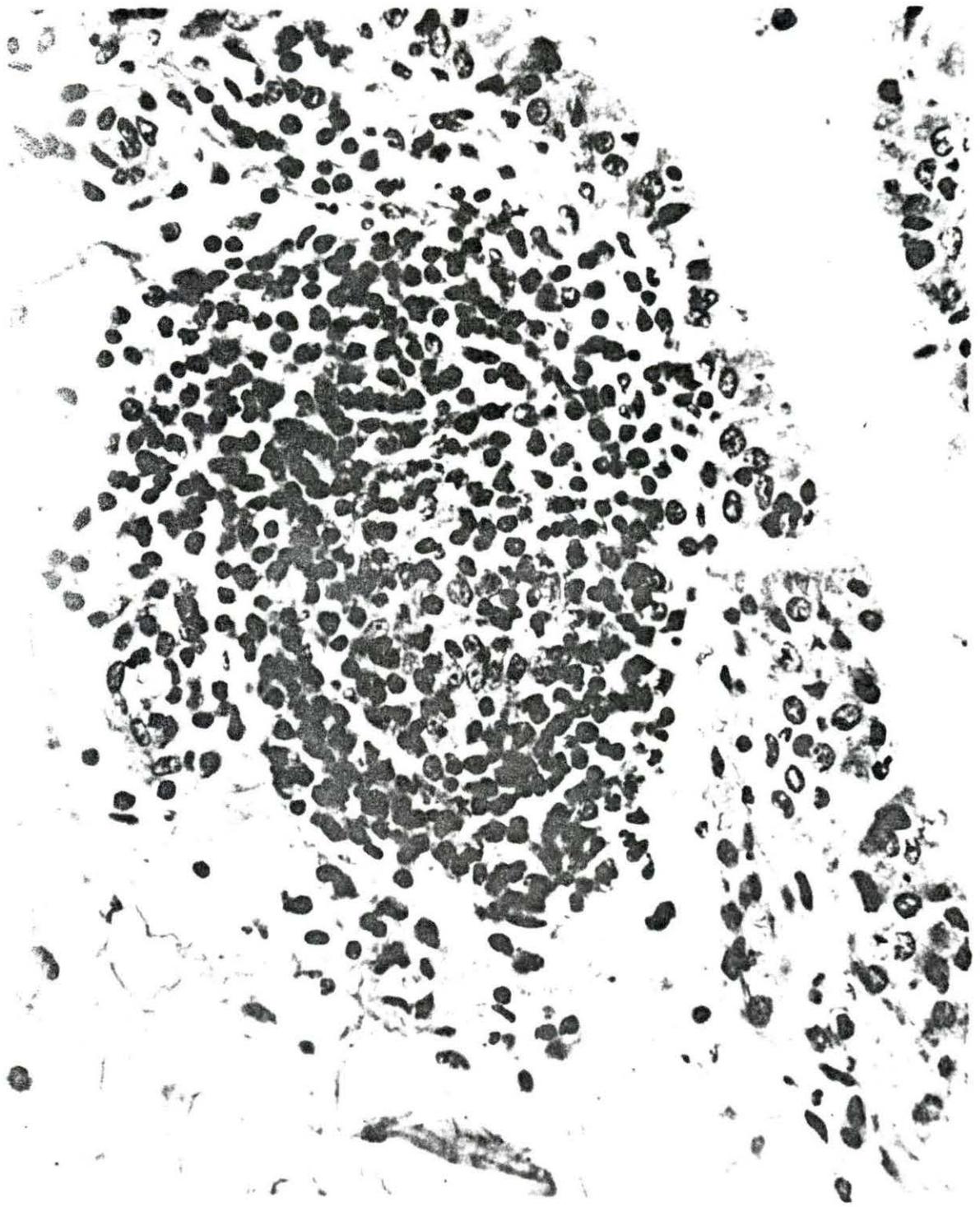
Groups 1 and 2

The bones of the animals necropsied 4 and 6 days post-inoculation appeared normal, histologically.

Group 3

Abnormal epiphyseal plate changes were observed in animal number 18 when necropsied 10 days after infection. All bones which were sectioned exhibited a disruption in the orderly formation of chondrocytes in the vesicular zone of the epiphyseal cartilage. There was a marked tendency for the chondrocytes to clump, thus causing the calcified trabeculae to be very irregular, thin and lattice-work-like in shape (Figures 22, 24). The osteoblast and endothelial cell activity appeared to be normal. All animals exhibited an increase of eosinophiles and neutrophiles in the periosteum of the fifth rib sectioned (Figure 33). Considerable inflammatory exudate was present on the parietal pleura of the infected animals.

Group 4

Animal 21 in group 4 exhibited changes similar to those described for group 3. In addition the lattice-work-like trabeculae close to the epiphyseal plate had osteoid borders, whereas in the control animals definite osteoid borders were not present on the trabeculae adjacent to the epiphyseal plate. Rib changes similar to those described for group 3 were observed in all inoculated animals.

Group 5

Histopathological changes in the animals of group 5 resembled those described for the animals in the 10-day group. In addition there was a broadening of the epiphyseal plate and a decreased endothelial cell and osteoblast activity. Animal number 30 exhibited extensive fibrous pleural adhesions and an infiltration of neutrophiles and eosinophiles into the periosteum of the fifth rib. The infiltrating cell of the periosteum was similar to that observed in the animals of group 3. Some of the control animals also exhibited this cellular change in the periosteum even though the pleura was normal.

Group 6

Marked changes of osteoporosis and osteolysis were present in the animals necropsied 56 days postinoculation. The proximal end of the radius of animal 33 showed a reduction in the thickness of the bony trabeculae and epiphyseal plate whereas no osteoporotic changes were present in the same area of the opposite leg (Figures 25, 26, 27). A large pannus covered the articular surface of the radius in animal 33. The fibrous mass was highly vascularized and infiltrated with lymphocytes and plasma cells. An area of hyaline necrosis of the fibrous mass was present at the site of attachment to the distal end of the humerus. In areas of attachment of the pannus to the articular surface of the radius, metaplasia of the hyaline cartilage to fibrous connective tissue had

occurred. Osteolysis of the bony spicules adjacent to the
articular cartilage appeared to be occurring as the result of
the action of stellate mononuclear cells (Figure 28). The
osteolytic process had progressed almost to the epiphyseal
plate. In the area of osteolysis the nuclei of the osteocytes
were quite large and in many instances there were pronounced
lacunae around the osteocytes. This was in contrast to the
normal nuclei of the osteocytes which were quite pyknotic.
Several areas of vascular penetration of the epiphyseal plate
adjacent to the deepest penetration of the pannus had occurred.

In animal 34 the 4 bones which were sectioned exhibited
histopathological changes. Endothelial cell activity was
suppressed and the osteoblasts were stellate in morphology.
There was hypoplasia and hyperemia of the bone marrow (Figure
29). Osteoclasts were present in the fibrous layer of the
periosteum (Figure 30). Disorganization of the zone of ma-
turing cartilage cells similar to the previous groups was
present. The epiphyseal plate of the proximal end of both
radiuses was very thin. In many areas of the epiphyseal plate
there were few cartilage cells in the zone of maturing carti-
lage cells and the endothelial cell invasion of cartilage and
osteoblastic activity was reduced (Figure 32). Control ani-
mals of group 6 exhibited a slower endothelial cell invasion
when compared with the control animals of other groups. This
was evidenced by osteoid borders on the trabeculae adjacent to
the vesicular zone of the epiphyseal plate.

The control animals, as well as most of the inoculated animals, exhibited neutrophiles and eosinophiles in the periosteum of the rib.

Changes of the Lung and Pleura

No gross pathological change of the lungs or pleura was observed in group 1. The pleural surface of all inoculated animals of group 2 was covered with a fibrino-purulent exudate. The nonadherent exudate was especially prominent at the margins of the lungs and between the diaphragmatic lobes of the lung and the diaphragm.

All infected animals necropsied 10 days postinoculation exhibited similar pleural changes with the exception that the exudate was more abundant.

A fibrino-purulent pleuritis was observed in the animals necropsied 15 days postinoculation, but was less extensive than that observed in the infected animals examined 10 days postinoculation.

Pleural adhesions were noted in all infected animals of group 5 (Figure 34). Animal 28 had extensive pleural adhesions of the left cardiac, right apical, right cardiac and the right diaphragmatic lobes of the lungs. The lungs appeared normal in color and no evidence of pneumonia was present.

Animal 34 of group 6 had fibrous pleural adhesions of all lobes of the lungs. Marked hyperemia was present around these adhesions. Other animals of this group exhibited organized

Figure 20. The articular cartilage of the coxo-femoral
joint of animal 34 was soft and easily detached
from the subchondral bone. 56 days postinocu-
lation.

Figure 21.   The epiphyseal plate of control animal 19.
             Note the orderly maturation pattern of the
             chondrocyte columns and the resulting rela-
             tively straight trabeculae of the primary
             spongiosa. 10 days postinoculation. Lillie's
             allochrome stain. X 60.

Figure 22.   The epiphyseal plate of animal 21. Note the
             disruption in the orderly maturation of the
             chondrocyte columns. The calcified trabeculae
             are lattice-work-like in appearance and some-
             what thinner than those of the control animal.
             10 days postinoculation. Lillie's allochrome
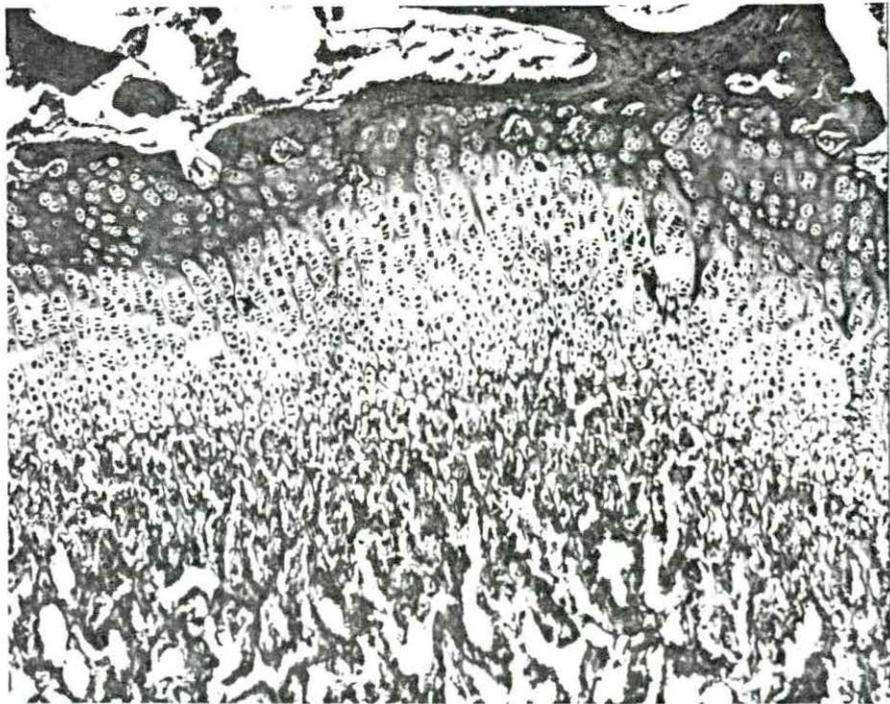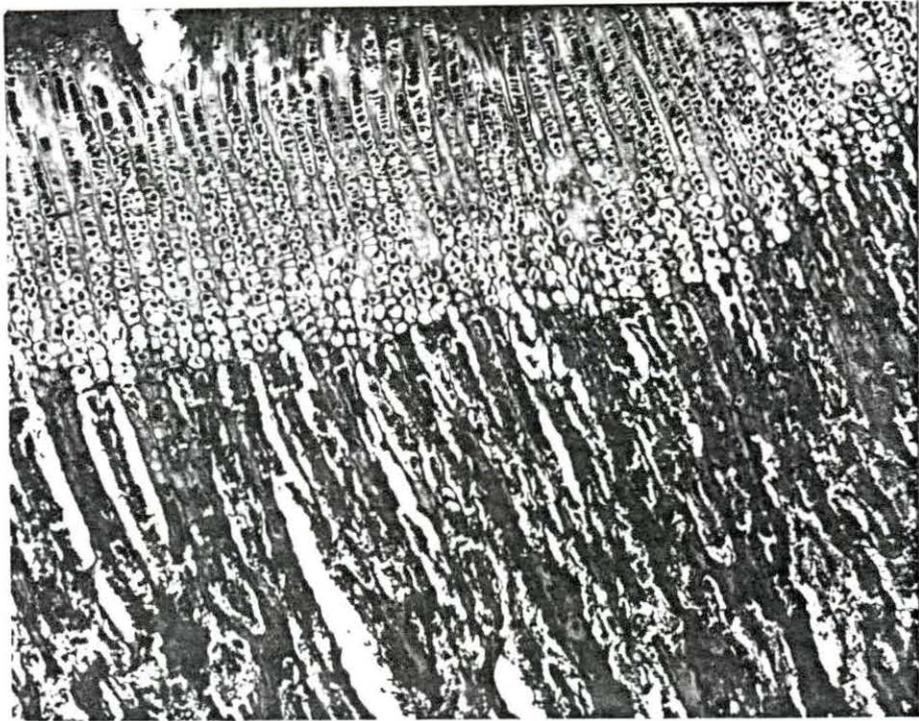   stain. X 60.

Figure 23. Higher magnification of Figure 21. 10 days
            postinoculation. Lillie's allochrome stain.
            X 160.

Figure 24. Higher magnification of Figure 22. 10 days
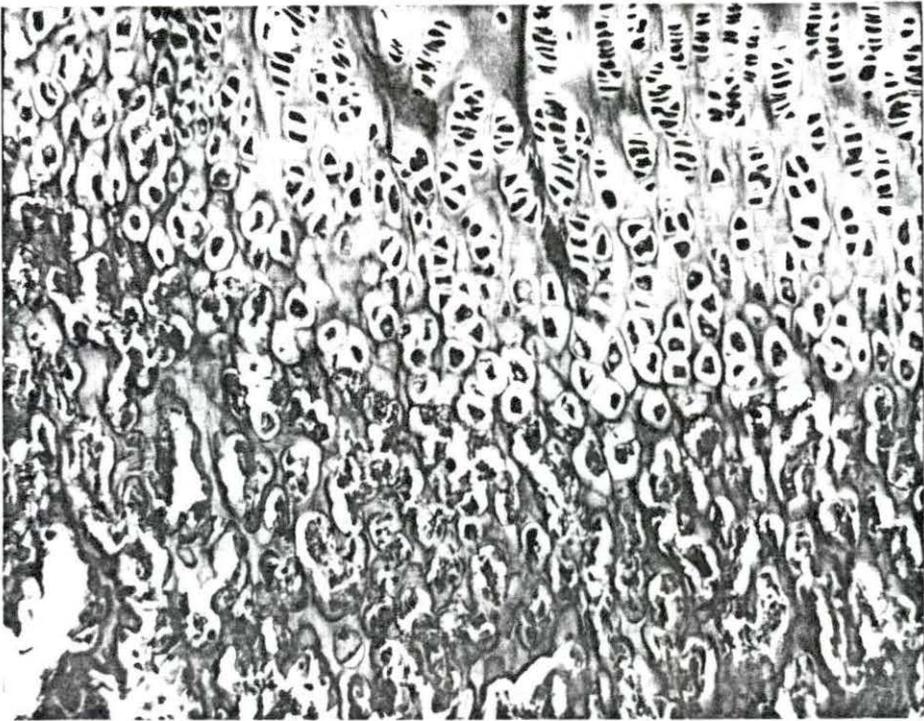   postinoculation. Lillie's allochrome stain.
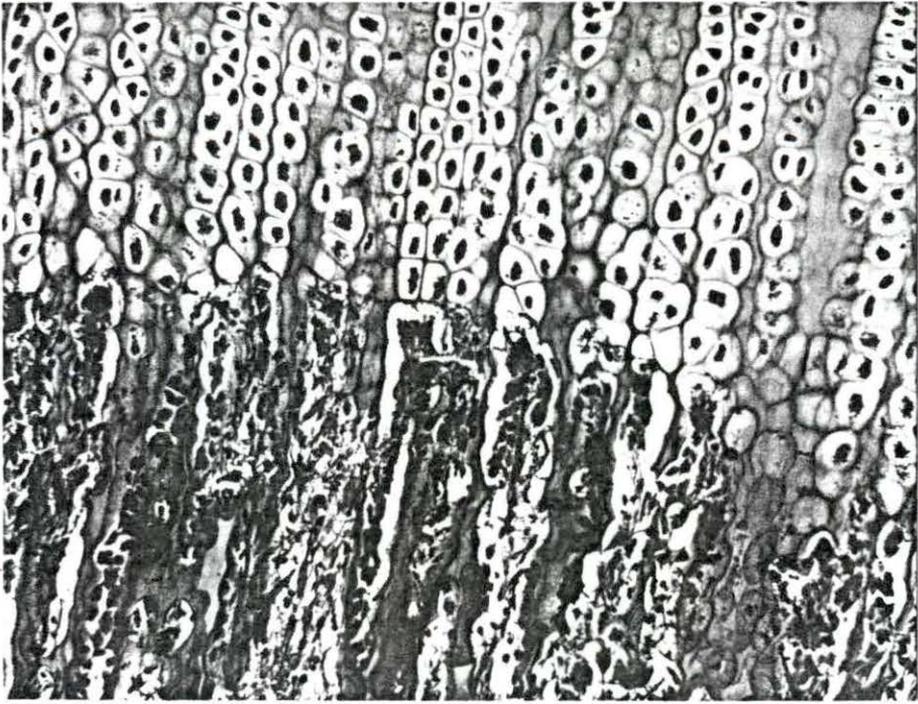   X 160.

Figure 25. Note the relatively normal epiphyseal plate
architecture of the proximal end of the left
radius of animal 33. 56 days postinoculation.
Lillie's allochrome stain. X 60.

Figure 26. Note the epiphyseal plate of the proximal end
of the right radius of animal 33. This is the
opposite leg sectioned at approximately the
same site as Figure 25. Note the thinning of
the epiphyseal plate and calcified trabeculae.
Vascular penetration of the epiphyseal plate
and relative inactivity of the zone of pro-
liferating chondrocytes. The animal did not
touch the right front foot to the ground for
3 weeks before necropsy. 56 days postinocula-
tion. Lillie's allochrome stain. X 60.

Figure 27.   Higher magnification of Figure 26.   56 days
postinoculation.   Lillie's allochrome stain.
X 160.

Figure 28. The articular surface of the proximal end of
            the right radius from animal 33. Note the
            pannus attachment to the articular surface (A)
            and beginning metaplasia of the cartilage to
            fibrous connective tissue (B). Also beginning
            osteolysis is present in spicules adjacent to
            the articular cartilage (C). 56 days postin-
            oculation. Hematoxylin and eosin stain.
            X 160.

Figure 29.   This is the bone marrow of animal 34.   Note the
            lack of hematopoietic tissue, reduced thickness
            of the boney spicules and hyperemia of the mar-
            row vessels.   56 days postinoculation.   Hema-
            toxylin and eosin.   X 60.

Figure 30.   The bone marrow and periosteum of the fifth rib
            from animal 34.   Note the lack of hematopoietic
            tissue, reduced thickness of the boney spicules
            and osteoclastic accumulations in the perios-
            teum.   56 days postinoculation.   Hematoxylin
            and eosin.   X 60.
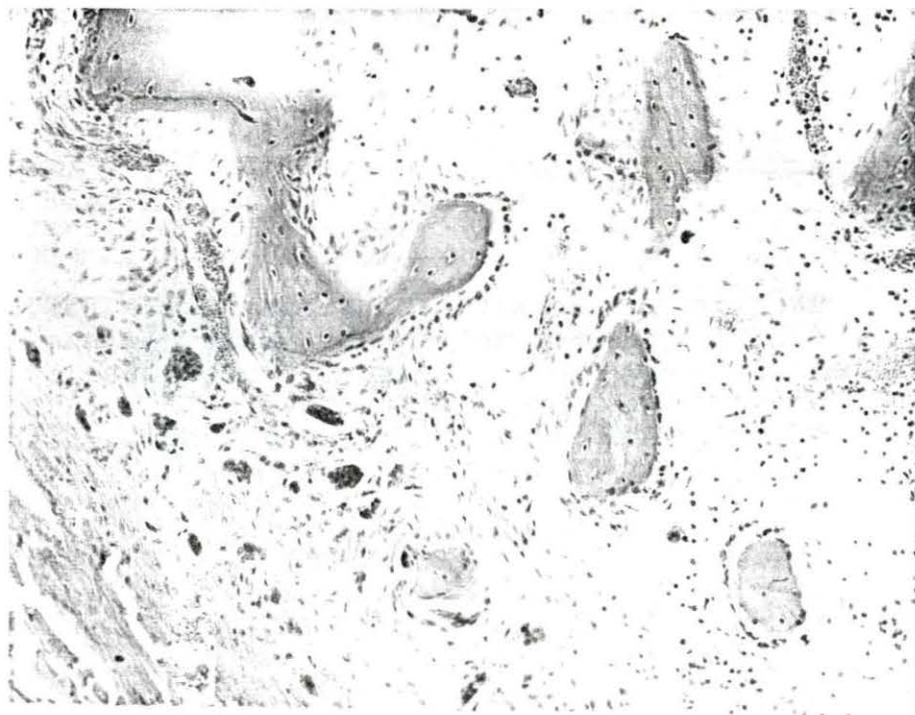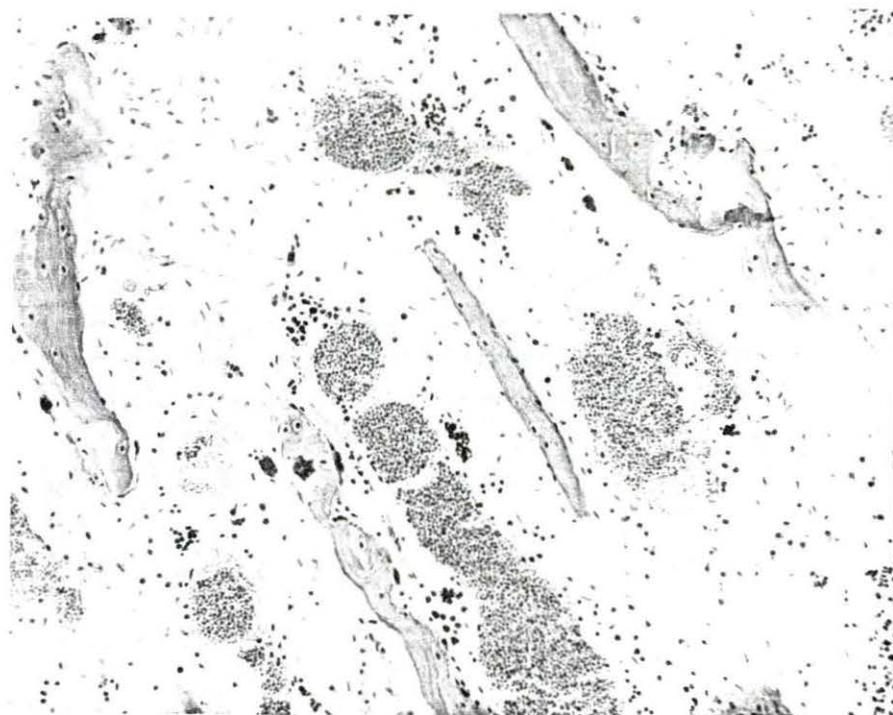
Figure 31.   This is the primary spongiosa of the fifth rib
             from control animal 36. The osteoblast appear
             cuboidal to stellate in morphology and are
             numerous. 56 days postinoculation. Hematoxylin
             and eosin. X 160.

Figure 32.   This is the primary spongiosa of the fifth rib
             from inoculated animal 34. Note how small the
             osteoblasts are. The nuclei are quite pyknotic
             and the cells appear inactive. 56 days post-
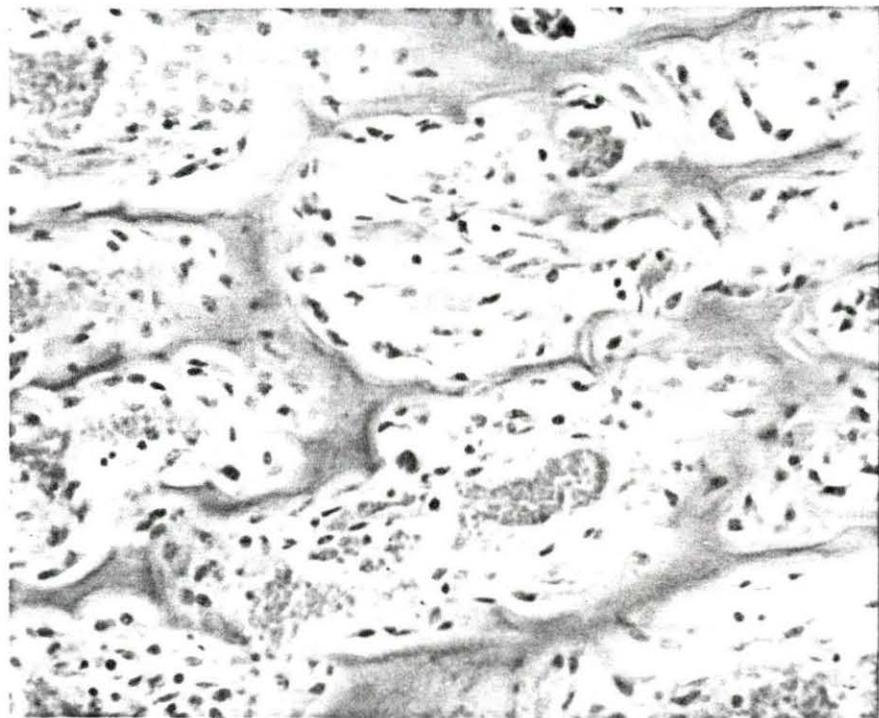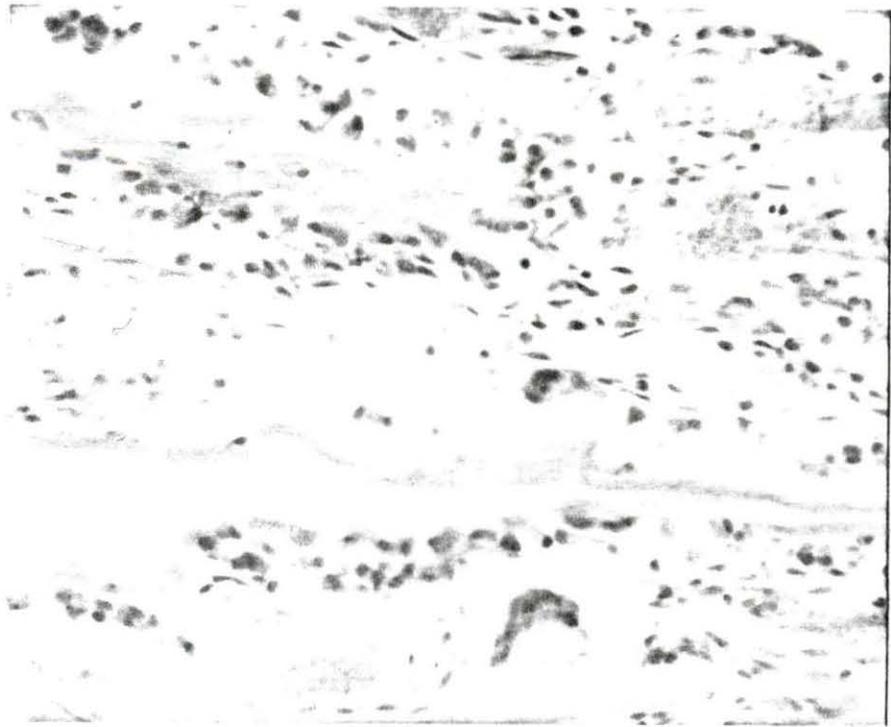   inoculation. Hematoxylin and eosin. X 160.

Figure 33. This is the periosteum from animal 26. Note
the accumulations of eosinophiles and neutro-
philes. These cellular accumulations were
observed in both the control and infected
animals at all sampling periods. 30 days post-
inoculation. Hematoxylin and eosin. X 160.

pleural adhesions but to a lesser degree.

Microscopically, the inflammatory changes of the lungs in all infected animals were confined to the pleural edges. The lungs from the animals of group 1 exhibited a scant pleural exudate composed primarily of macrophages, plasma cells and a few neutrophiles. Isolated foci composed of similar cell types were present in the pleura. Mild hyperemia of the pleura was present.

The pleural exudate was more abundant in animals at the 6-day sampling period than at the 4-day period. The more abundant exudate contained many neutrophiles. In some areas the pleural cells were swollen. The pleura was thickened primarily from an increase of macrophages, lymphocytes and plasma cells (Figure 36). Also, an occasional isolated focus of neutrophiles was present. The plasma cell and lymphocytic infiltration extended into the adjacent interalveolar spaces.

The fibrino-purulent pleuritis of inoculated animals of group 3 was very pronounced. The serosal cells were swollen and in many instances indistinguishable from macrophages (Figure 37). The pleura was thickened greatly by infiltration of macrophages, plasma cells and in some areas neutrophiles (Figure 38). A zone of plasma cells was present along the junction of the pleura and lung, and in some instances these cells penetrated the adjacent interalveolar spaces. Increased vascularization of the pleura had occurred.

The histopathological changes of group 4 resembled that

described for the 10-day group with the exception that the pleural exudate was scant (Figure 39).

The pleural exudate of group 5 was scant and composed of neutrophiles and macrophages. In some areas there was organization of the exudate. Where the pleural exudate was attached to the serosa, neutrophilic infiltration of the pleura was present. The lymphocytic accumulations of the pleura tended to be in isolated foci that were most frequently found at the junction of 2 pulmonary lobules (Figure 40). Occasionally, areas of extensive lymphocytic and plasma cell infiltration were present.

Fibrosis of the pleura was present in the inoculated animals of group 6. Many strands of fibrous connective tissue were present in areas of pleural adhesions (Figure 41). No cellular infiltration of the pleura or lung was present at this time. The lungs of all control animals remained normal.

Heart Lesions

The heart changes were limited to either a serous or a fibrinous pericarditis. No pericardial lesions were observed in either group 1 or group 2. Only 1 animal in group 3 had a 2-fold increase of pericardial fluid containing a few strands of fibrin.

All inoculated animals in group 4 exhibited a 2- to 4-fold increase in pericardial fluid. The pericardial sac of animal 22 was enlarged with a fibrinous exudate on the serous

Figure 34.   Extensive pleural adhesions were present in
             animal 30.   Note the relatively normal appear-
             ance of the lung tissue.   30 days postinocula-
             tion.

Figure 35.   A normal pleura of animal 13.   Note the squa-
mous type cell forming the serosal cell layer.
10 days postinoculation.   Hematoxylin and
eosin.   X 430.

Figure 36.   The inflammatory cellular change of the pleura
from animal 9.   Note the swelling of the sero-
sal cells, infiltration of the pleura by
plasma cells and mononuclear cells and plasma
cell accumulations in the adjacent interalveo-
lar interstitial spaces.   6 days postinocula-
tion.   Hematoxylin and eosin.   X 400.
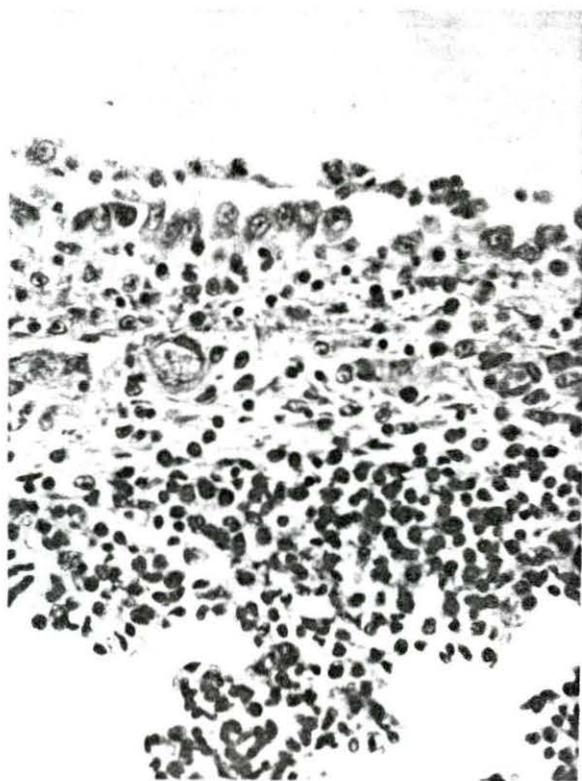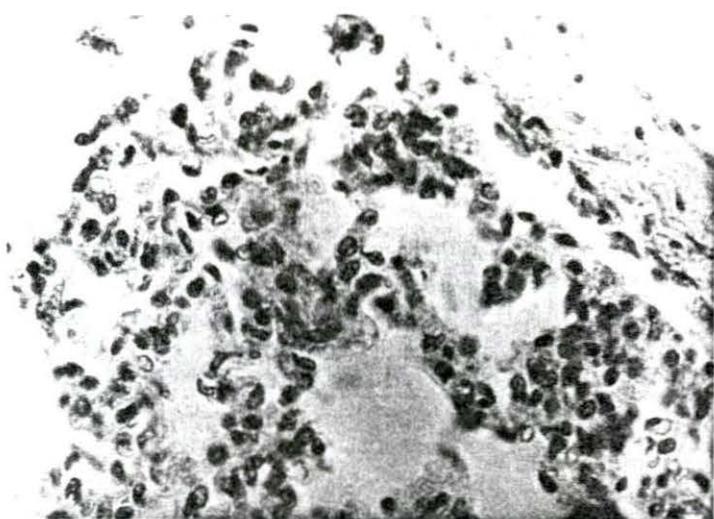
Figure 37.   Note the thick layer of fibrino-purulent
             pleural exudate (A), swelling of the serosal
             cells (B) and plasma cell infiltration of
             the pleura (C). Animal 21. 10 days post-
             inoculation. Hematoxylin and eosin. X 100.

Figure 38.   Note the plasma cell, lymphocyte and neutro-
             phile infiltration of the pleura when a
             fibrino-purulent exudate was attached to the
             serosal surface. 10 days postinoculation.
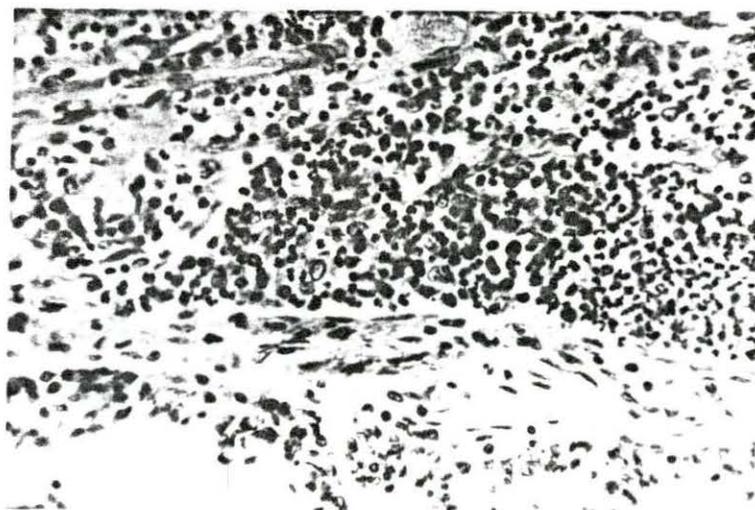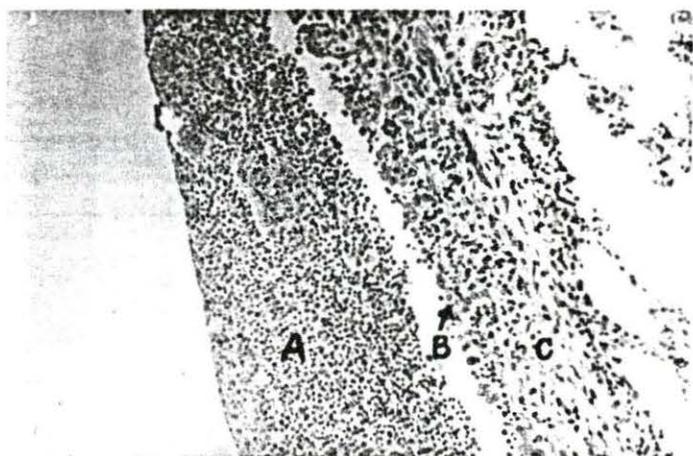   Hematoxylin and eosin. X 430.

Figure 39. Note the plasma cell and lymphocyte infiltra-
tion of the pleura in animal 22. 15 days
postinoculation. Hematoxylin and eosin. X 400.

Figure 40. At 30 days postinoculation the infiltrating
lymphocytes tended to accumulate in foci.
Animal 27. Hematoxylin and eosin. X 100.
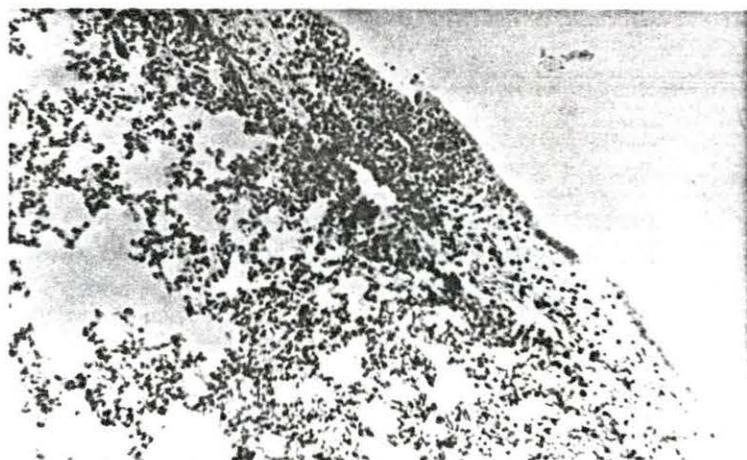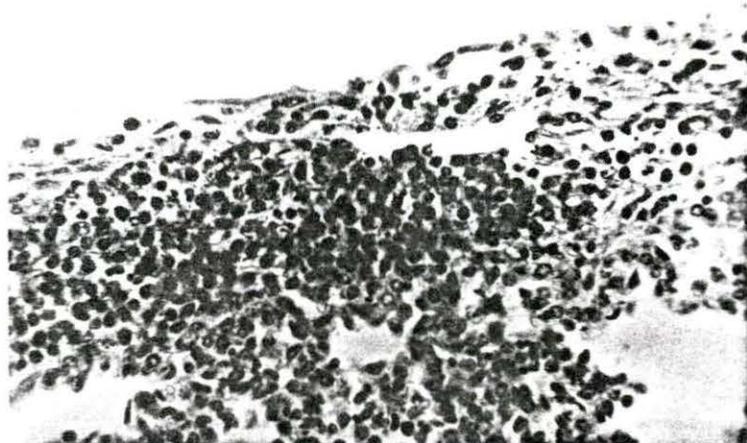
Figure 41. Organization of the pleural exudate with the formation of pleural adhesions in animal 34. Note the fibrillary surface of the pleura with minimal cellular infiltration. 56 days postinoculation. Hematoxylin and eosin. X 100.

Figure 42. Interlobular lymphocytic infiltration of the liver and Glisson's capsule from animal 12. 6 days postinoculation. Hematoxylin and eosin. X 160.
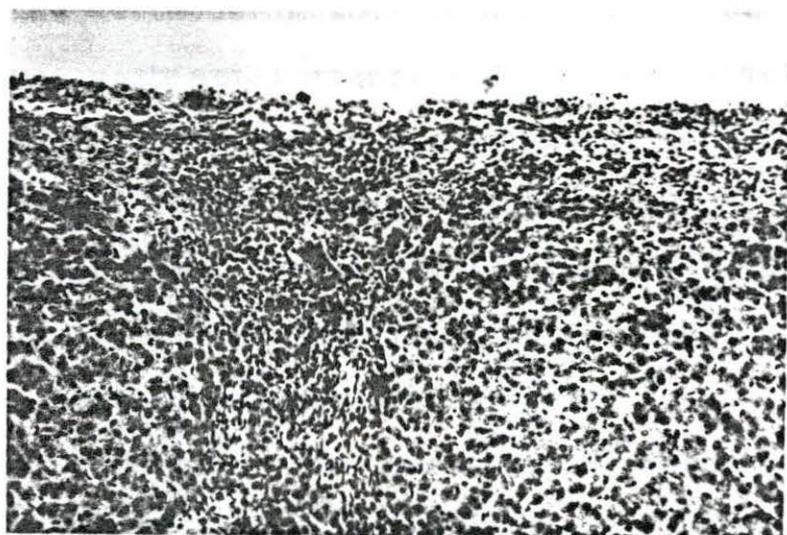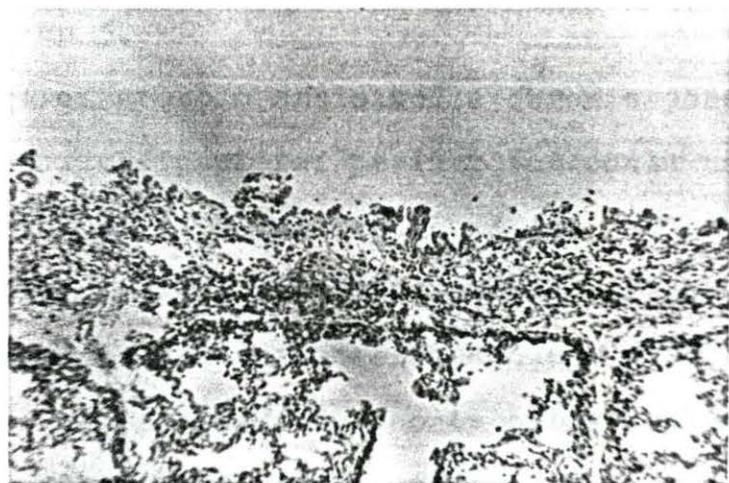
surface which was 5 to 15 millimeters in thickness (Figure 43).

No pericardial involvement was observed in the inoculated animals of group 5.

Animal 34 of group 6 exhibited a chronic constrictive pericarditis and the parietal pericardium could not be reflected from the heart. Animal 33 had a 2-fold increase in pericardial fluid which contained numerous flakes of fibrin.

No cellular change was observed in the pericardium or heart of animals which evidenced only an increase in pericardial fluid. Animal 22 of group 4 which exhibited a fibrinous pericarditis had an extensive layer of immature connective tissue on the epicardium with a thick layer of fibrin forming the frictional surfaces of the pericardium and epicardium. In the highly vascularized connective tissue layer many neutrophiles were present. Lymphocytes and connective tissue were seen infiltrating the perimuscular spaces. Many blood vessels near the epicardium exhibited thick cuffs of lymphocytes. Beneath the fibrin layer of the frictional surface an extensive zone of mainly undifferentiated mononuclear cells and plasma cells was present (Figures 44, 45). This cellular zone was present on both the pericardial and epicardial sides of the fibrin layer. Unfortunately, tissues of the fibrous pericarditis of animal 34 were not examined histologically.

Figure 43.   A fibrinous pericarditis from animal 15 at 15 days postinoculation.
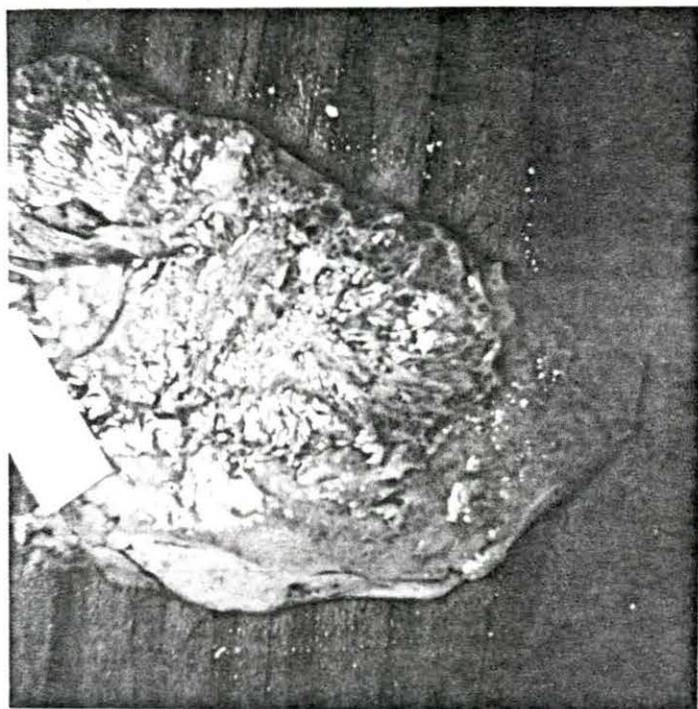
Figure 44.   Pericarditis from animal 22.   Note the myo-
             cardium (A), zone of immature connective
             tissue (B) and an extensive zone of lympho-
             cytes and plasma cells (C).   15 days post-
             inoculation.   Hematoxylin and eosin.   X 60.

Figure 45.   Higher magnification of Figure 44 showing the
             zone of lymphocytes and plasma cells.   15
             days postinoculation.   Hematoxylin and eosin.
             X 160.
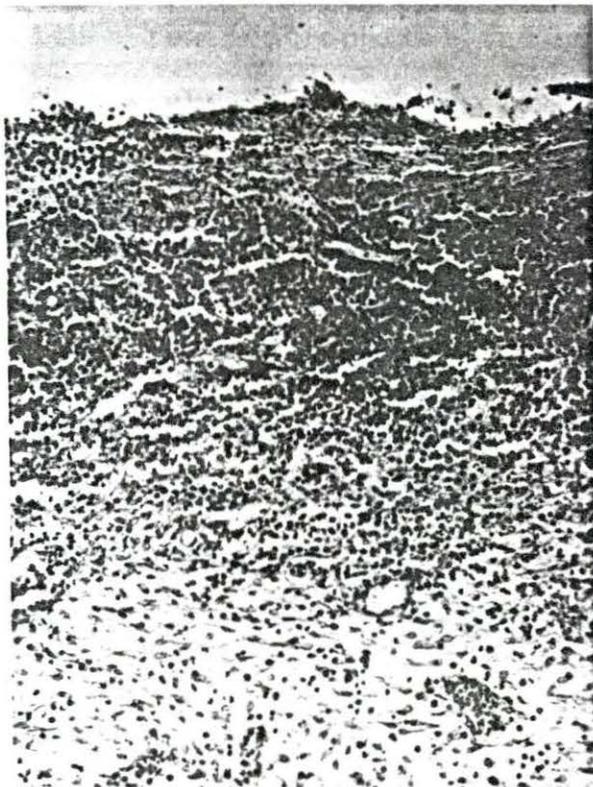
Liver Lesions

All infected animals of groups 1, 2 and 3 exhibited a
fibrino-purulent peritonitis (Figure 46). The exudate was
scant in the infected animals of group 1, becoming more abun-
dant in the animals of group 3. It was nonadherent and promi-
nent at the margins of the liver and between the diaphragm
and liver. Only tags of fibrin were present over the visceral
surfaces of the abdominal organs in the animals of group 5.
There were fatty degenerative changes in the liver in animal
34 of group 6.

The serosal cells of all animals of group 1 were swollen.
Glisson's capsule was infiltrated primarily by plasma cells
and lymphocytes with a few neutrophiles and eosinophiles. In
many areas the inflammatory cellular change had extended into
the parenchyma of the liver. In these areas necrosis of the
hepatic cells was present as evidenced by karyorrhexis of the
nuclei. There were focal areas of lymphocytic infiltration in
the sinusoids of the liver in animals 4 and 5. These changes
were accompanied by necrosis of adjacent hepatic cells. Peri-
vascular lymphocytic cuffing of the vessels of the portal
areas was present in animal 4. The peritoneal exudate in this
animal was scant and composed of lymphocytes, macrophages and
neutrophiles.

The animals in group 2 evidenced a thickening of Glisson's
capsule due to infiltration of primarily large and small

mononuclear cells and plasma cells (Figure 42). Lymphocytes had also infiltrated the parenchyma of the liver. The peritoneal exudate was composed primarily of fibrin, neutrophiles and a few lymphocytes.

Group 3 exhibited changes similar to those observed at the 6-day sampling except that the peritoneal exudate was more abundant and fibrinous.

Focal lymphocytic accumulations in Glisson's capsule were present in the infected animals of group 4, especially at the interlobular spaces. Organization of the serosal exudate was beginning. Immature fibroblasts were extending into the peritoneal exudate which was extensively infiltrated with neutrophiles.

The only microscopic change in the hepatic tissue of the animals of group 5 was a focal infiltration of lymphocytes at the interlobular space of Glisson's capsule. Fibrosis of the capsule was minimal.

Animal 34 of group 6 exhibited fatty degenerative changes of the hepatic cells. No other microscopic lesions were observed at this sampling period.

Spleen Lesions

The gross changes of the spleen were confined to the serosal surface and closely resembled those described as occurring in the liver.

Histopathological examination of the tissues from all

Figure 46. Note the fibrino-purulent exudate at the
margins of the liver in animal 11. 6 days
postinoculation.
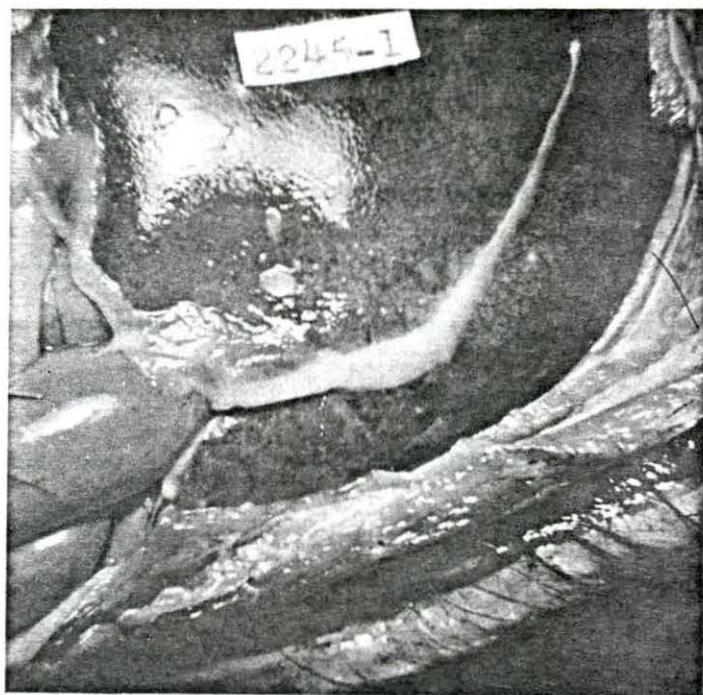
infected animals of group 1 revealed swelling of the serosal
cells and infiltration of the peritoneum and capsule by lym-
phocytes and plasma cells. The peritoneal exudate at this
time was scant and composed of macrophages and neutrophiles.

At 6 days postinoculation the peritoneal exudate of all
animals was composed principally of neutrophiles, fibrin and
a few macrophages. Swelling of the serosal cells was present.
Intermingled with the lymphocytes in the capsular spaces were
macrophages which had a very large nucleus with minimal chro-
matin structure.

Enlargement of the serosal cells, infiltration of the
subperitoneal space by lymphocytes, and beginning capillary
invasion of the peritoneal exudate had occurred in group 4.

The peritoneal surface of all infected animals of group 5
had a very rough and frayed appearance. Isolated foci of lym-
phocytes were present in the subperitoneal space, whereas in
other areas organization of the peritoneal exudate was pres-
ent.

No pathological change was observed in group 6.

Lymph Node Lesions

In the animals of groups 1 and 2 the gross changes of the
lymph nodes were confined to the anterior mediastinal lymph
nodes. These were enlarged and edematous.

The internal iliac lymph nodes were enlarged, edematous
and hyperemic in the infected animals of groups 3, 4, 5 and 6

when the corresponding coxo-femoral or femoro-tibial joint was
involved.   The popliteal nodes were enlarged when the hock
joints were involved.

In all groups the anterior mediastinal and the internal
iliac lymph nodes were affected similarly.   In the infected
animals of group 5 the anterior mediastinal and internal iliac
lymph nodes were enlarged 4 to 5 times their normal size (Fig-
ure 47).   They were firm and somewhat edematous with periph-
eral hyperemia.

Microscopically, there was proliferation of the reticulo-
endothelial cells and infiltration of many neutrophiles into
the sinusoids of the anterior mediastinal lymph nodes of all
infected animals of group 1.   Edema of the lymph nodes was
present.   Similar changes were present in the involved ante-
rior mediastinal and internal iliac lymph nodes of groups 3,
4, 5 and 6.

Testicle Lesions

The gross changes of the testicle and scrotal cavity
closely paralleled those described for other visceral surfaces.
All infected male animals with involvement of the peritoneal
surfaces had the scrotal cavity affected with similar changes
(Figure 48).   The gross changes varied from fibrino-purulent
exudate in the scrotal cavity to organization of the exudate
and formation of scrotal adhesions.   Such adhesions were
observed in the male animals of groups 5 and 6.   The fibrino-

Figure 47.   A serous lymphadenitis of animal 29 was
present.   Note the enlargement, pericapsular
edema and hyperemia of the lymph nodes.   30
days postinoculation.
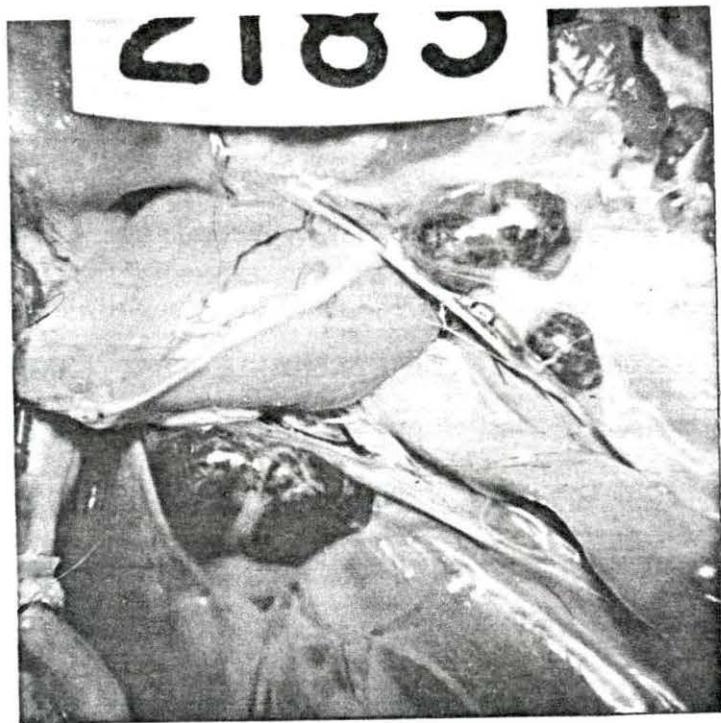
purulent exudate was especially prominent around the epididymis and spermatic cord.

In group 1 the inflammatory exudate in the scrotal cavities of the 2 male animals was composed of macrophages, lymphocytes and neutrophiles. The blood vessels of the tunica vaginalis propria and communis were hyperemic and perivascular lymphocytes were present. At 6 days postinoculation similar changes were observed in 3 male animals. Fibrino-purulent exudate of the scrotal cavity was marked in groups 3 (2 males) and 4 (3 males) and was composed primarily of fibrin and neutrophiles. Hyperemia of the tunica vaginalis communis and propria was present and perivascular lymphocytic cuffing was marked. Neutrophilic and lymphocytic infiltration throughout these layers were present (Figure 49). Neutrophiles were numerous around many seminiferous tubules at 10 and 15 days postinoculation and in some instances the neutrophiles were infiltrating the lumen of the tubules (Figure 50). Areas of fibrous adhesions were present in 1 male in group 5 and in 2 males in group 6.

Brain Lesions

Only the brain of animal 34 exhibited gross pathological changes. The cerebrospinal fluid was very turbid and contained large flakes of fibrin. The meningeal surface of the brain was quite hyperemic.

Histopathologically, a leptomeningitis was present in

this animal. The subarachnoid space was packed with lympho-
cytes (Figure 52). A large area of compression necrosis was
present in the cerebral cortex which apparently resulted from
massive focal accumulations of exudate in the subarachnoid
space (Figure 51). The necrotic area was outlined by a zone
of gliosis. In many areas of the subarachnoid space, lympho-
cytes accompanied the arteries for a short distance into the
cerebral cortex. Both infected and control animals exhibited
large accumulations of oligodendrocytes adjacent to the lat-
eral ventricle.

Kidney and Adrenal Gland Lesions

Neither gross nor microscopic alteration was observed in
either the kidneys or the adrenal glands of the inoculated
animals.

Figure 48.   A fibrino-purulent exudate was present in the
             scrotal cavity of animal 21. Note that the
             exudate was especially prominent over the
             spermatic cord. 15 days postinoculation.
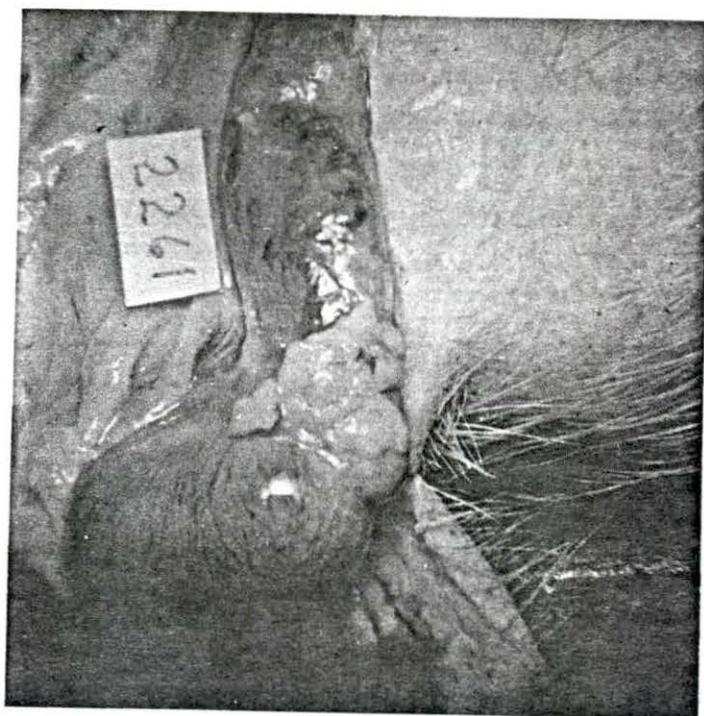
Figure 49.   Purulent exudate observed in the scrotal cavity
             of animal 23.   Note the extension of the inflam-
             matory change into the tunica vaginalis commu-
             nis.   15 days postinoculation.   Hematoxylin and
             eosin.   X 100.

Figure 50.   Infiltration of neutrophiles in the peri-
             tubular spaces of the testicle of animal 23.
             15 days postinoculation.   Hematoxylin and
             eosin.   X 100.
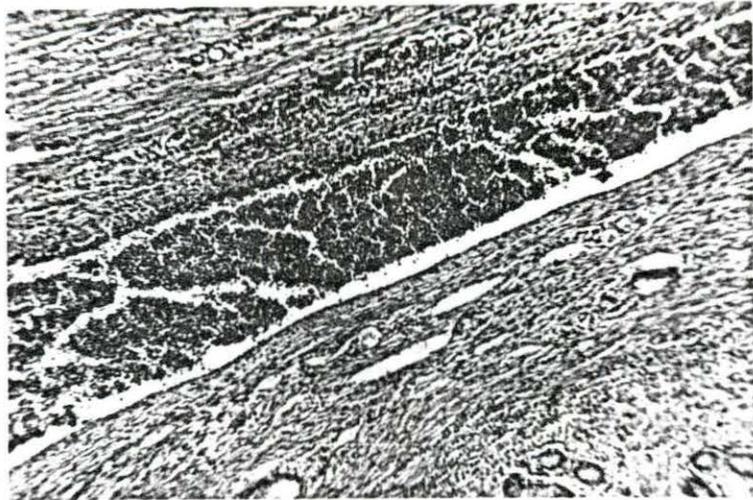
Figure 51.   Brain of animal 34 with compression necrosis
              of the cerebral cortex demonstrates a zone of
              gliosis (A), area of compression necrosis (B)
              and the leptomeningitis the cell type of which
              is predominantly lymphocytes. 56 days post-
              inoculation. Hematoxylin and eosin. X 430.

Figure 52.   Lymphocytic leptomeningitis in animal 34. 56
              days postinoculation. Hematoxylin and eosin.
              X 430.
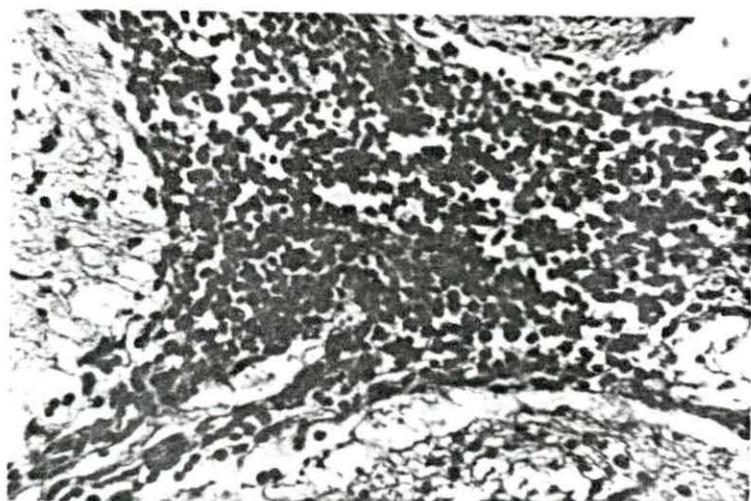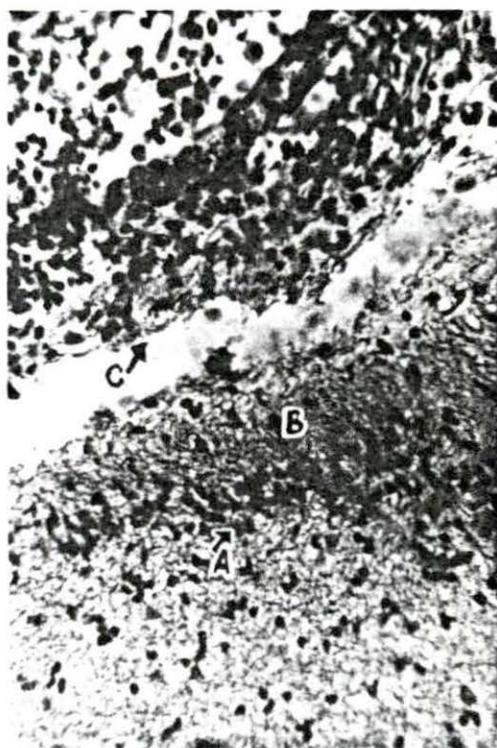
DISCUSSION

Klieneberger (33) states that Mycoplasma sp. infections in animals vary in their host effect and that a natural infection does not readily follow exposure to the organism. Switzer (71) noted that M. hyorhinis has a particular affinity for the serous membranes during the septicemic phase of this organism. Frequently, the joints may become affected with resultant lameness and stiffness.

Intraperitoneal inoculation of M. hyorhinis isolate SK76 into young pigs proved to be a satisfactory system for the production of arthritis due to this organism. This technique produced a septicemia in many of the pigs as evidenced by the recovery of the organism from the blood (Table 2). All pigs inoculated intraperitoneally with M. hyorhinis developed a rough coat approximately 3 days postinoculation. Possibly, this was associated with inflammatory changes of the pleural and peritoneal surfaces. Such inflammatory changes were observed in the pigs which were necropsied 4 and 6 days postinoculation. The synovial membranes showed minimal involvement at this time. Definite symptoms of lameness developed several days after the appearance of the roughened hair coat. This sequence of events, as postulated by Switzer (71), suggests that the organism localized first on the serosal surfaces with the synovial membrane invaded at a later time.

In many animals the lameness was minimal, lasting only a

few days, whereas in other animals the lameness persisted throughout the experiment. In one animal, number 33, lameness occurred early in the trial, disappeared and then reoccurred 28 days postinoculation. This is not in accord with the observation of McNutt (41) who found that M. hyorhinis arthritis was continuous, without remissions or exacerbations. Even though animals 27 and 37 necropsied 10 days postinoculation did not develop marked symptoms of lameness, involvement of some of the synovial membranes was present.

The gross involvement of the intact joint in general varied from puffiness to mild periarticular fibrosis. The extensive periarticular fibrosis reported by McNutt (41), McNutt et al., (42), Willigan (74) and Willigan and Beamer (75) was not observed in any of the infected animals.

Marked hyperemia of the synovial membranes was observed first in pigs necropsied 10 days postinoculation. Fifteen days postinoculation, scant hyperemia of the synovial membrane was observed. However, copious amounts of muco-fibrinous synovia were present. At 30 and 56 days postinoculation, the coloration of the involved synovial membrane was yellowish and was, occasionally, accompanied by a marked hyperemia. The yellowish coloration and marked hyperemia could be observed in different joints of the same animal. Hyperemia of the synovial membrane in cases of M. hyorhinis arthritis has been reported by McNutt (41), McNutt et al., (42), Willigan (74), Willigan and Beamer (75) and Switzer (70, 71) whereas the

yellowish coloration of the more chronically involved joints
was not reported by these workers.

The early synovial membrane changes consisted of hyper-
emia, plasma cell and lymphocytic infiltration and fibrin
formation on the surface of a few of the more acutely involved
membranes. By 30 and 56 days postinoculation the lymphocyte
had replaced the plasma cells as the predominant inflammatory
cell. In all sampling periods, the neutrophiles were associ-
ated with the presence of fibrin on the surface of the mem-
brane. McNutt (41) states that M. hyorhinis does not produce
polymorphonuclear leukocytic infiltration unless necrosis
occurs. The results observed in this study suggest that
fibrin formation is more closely associated with neutrophilic
infiltration than necrosis is.

A mild hyperplasia of the synovial villi which imparted
a velvety appearance to the synovial membrane was first ob-
served at 15 days postinoculation. The villi became more
prominent as the disease progressed, reaching maximum size at
30 days postinoculation. Hyperplasia of the synovial cells
occurred simultaneously with that of hypertrophy of the villi.
A mild increase in connective tissue was first observed in the
synovial villi of animals at 15 days postinoculation and was
confined to that region. These findings are not in accord
with McNutt et al., (42) and O'Donoghue et al., (48) who state
that the cellular changes of the synovial membrane are incon-
sistent and inconclusive. Later, however, McNutt (41)

reported that proliferative changes in and hyperemia of the synovial membrane had occurred. Also, he noted that very few inflammatory cells were present, but of those which were present the mononuclear leukocyte predominated. These synovial membrane changes reported by McNutt (41) are similar to the changes observed in the mildly affected synovial membranes which were examined in this study.

The cellular components of the synovial fluid consisted primarily of neutrophiles. These neutrophiles became apparent at the time of the first appearance of the gross lesions of the synovial membrane. The synovia was turbid, mucinous and increased in amount at 10 days postinoculation. The relative amount of synovia increased at later sampling periods. At all sampling periods M. hyorhinis was consistently isolated from grossly involved joints.

The bone changes which were associated with M. hyorhinis infection have not been reported elsewhere. These bone changes consisted of alterations associated with interference in the orderly maturation of the epiphyseal cartilage, and alterations associated with disuse atrophy and osteoporosis. This latter condition was associated with generalized debilitation. In addition there was osteolysis associated with pannus formation.

The interference with the orderly maturation of the epiphyseal cartilage cells consisted of disorganization of the vesicular zone of cartilage cells which resulted in distorted

trabeculae formation. This change was first seen at 10 days postinoculation in animal 18 and to some degree in most other inoculated animals sampled at subsequent periods. Whether M. hyorhinis interfered with the assimilation of nutrients which resulted in a disorganization of the cartilage cells of the vesicular zone or whether this is the direct result of M. hyorhinis is difficult to determine. The possibility exists that a moderate reduction in feed consumption may have occurred even though none of the inoculated animals was noticeably off feed. Frandsen et al., (20) stated that cartilage activity is a critical index of the nutrition of the animal and that nutritional deficiencies result in retardation of epiphyseal and costal cartilage cell proliferation. Dunne et al., (16) state that in acute hog cholera the bone changes consist of disorganization of the cartilage cells in the vesicular zone and an increase in the number of cartilage cells within the enlarged lacunae. With this information in mind it appears that the change occurring in the vesicular zone is a nonspecific change associated with an acute illness.

The bone changes which were present in the proximal end of the right radius of animal number 33 consisted of a thinning of the epiphyseal plate as evidenced by a lack of proliferating cartilage cells, a lack of osteoblastic activity and by osteoporosis. Since the animal did not touch the right front foot to the ground for 3 weeks prior to necropsy, these changes are interpreted as evidence of disuse atrophy. The

corresponding bone in the opposite leg was relatively normal.
Smith and Jones (65) state that osteoporosis occurs following
disuse of a limb. The vascular penetration of the epiphyseal
plate observed in animal 33 appears to be a regenerative
response to a severe irritation of the articular surface.
Luck (38) describes a similar change when necrosis of the
articular surface occurs. He states that necrotic elements of
bone and cartilage are invaded by vessels from the metaphyseal
region. These changes resemble those observed in this experi-
mental pig.

The gross lesions of the pleural surface were first
observed in the animals necropsied 6 days after they were
inoculated. These gross lesions consisted of a mild pleuritis
associated with a fibrino-purulent pleural exudate. At 10
days postinoculation a more extensive fibrino-purulent pleu-
ritis was associated with exudate accumulations. In many
areas, accumulations were as much as 1 centimeter in thick-
ness. The organized pleural adhesions were first observed in
the group of animals necropsied 30 days after the infection
occurred. Similar organized pleural adhesions were evident in
the pigs which were examined 56 days after inoculation. In
all of the inoculated animals, the gross pulmonary lesions
were confined to the pleural surface. An adequate confirma-
tion of the report by Runnells et al., (53) that M. hyorhinis
causes a primary pneumonia cannot be made at this time because
the animals were inoculated intraperitoneally only and, thus,

the organism was not localized in the respiratory tree. However, the intraperitoneal inoculation of M. hyorhinis does produce a septicemia and affords the organism an opportunity to invade the lungs if it has such capabilities. The intraperitoneal inoculation of the organism which was used in this research did not produce a primary pneumonia.

In groups 1 through 5 the inflammatory cellular reaction of the pleura consisted primarily of macrophage and lymphocytic infiltration, except in areas where the pleural exudate was attached to the pleura. The neutrophiles were abundant at these focal points. In most instances the inflammatory cellular response extended into the interstitial space of the alveoli adjacent to the pleura. By 30 days postinoculation, the lymphocytes were in isolated foci especially in areas which were adjacent to an interlobular space. The lymphoid cellular response of the pleura which was reported by Carter and Schroeder (4) was observed in the animals in groups 1 through 5. In addition neutrophiles were present when fibrin was attached to the pleural surface. This work is in accord with Carter and Schroeder (4) who state that a primary pneumonia could not be established with an intraperitoneal inoculation of M. hyorhinis.

Pericardial involvement was noted in 2 of 24 inoculated animals. This lesion consisted of a subacute fibrinous pericarditis and a chronic constrictive pericarditis. Switzer (69) states that a pericarditis is the most common lesion

observed in an M. hyorhinis infection. The present work indi-
cates that this may depend upon the particular strain of M.
hyorhinis present since the strain used in this experiment
produced microscopic synovial membrane lesions in 16 of 24
animals and a pericarditis in only 2 animals.

The gross lesions of the liver and spleen were those
which resulted from a fibrino-purulent peritonitis. Histo-
pathologically, the lesions were characterized by a swelling
of the serosal cells and by a peritoneal exudate composed pri-
marily of neutrophiles, fibrin, macrophages and a few lympho-
cytes. In both organs the inflammatory cellular change
consisted of lymphocytes and macrophages and extended into the
organs from the peritoneal surface. This indicates that M.
hyorhinis infection invades the serosal surface and is capable
of penetrating a short distance into any organ that has a
serosal surface. The fatty degenerative changes which were
present in the liver of animal 34 were probably caused by the
extreme debilitation of the animal. The depletion of lympho-
cytes in the spleen, as reported by McNutt (41), was not
observed in this study.

The pathological changes of the testicle and of the scro-
tal serosa closely paralleled those changes which were ob-
served in the visceral organs. The inflammatory changes
appeared to be confined to the tunica vaginalis communis and
propria, except in the animals which were necropsied 10 and 15
days after inoculation. In the latter 2 groups a peritubular

neutrophilic infiltration was present. In some areas the neutrophiles were present in the lumen of the tubules. Merchant and Packer (43) mention that semen and gravid uteri did not yield M. hyorhinis. This work, however, suggests the possibility of this organism being transmitted in the semen. The presence of scrotal adhesions at the time of castration should arouse suspicion that the herd has been infected with M. hyorhinis. Apparently, this is the first report of scrotal and testicular lesions occurring in M. hyorhinis infection.

An inflammatory enlargement of the anterior mediastinal, internal iliac and popliteal lymph nodes corresponds to the involvement of the pleura and the joints. Histopathologically, the changes consisted of reticulo-endothelial cell hyperplasia, edema and sinusoid infiltration by neutrophiles. Such changes are characteristic of a serous lymphadenitis. These changes correspond to the observation of Ducksbury (15) who reported that the involvement of the internal iliac nodes indicated the presence of arthritis in the corresponding coxofemoral or femoro-tibial joint.

The brain lesion which was observed in animal 34 is of a type that has hitherto been unreported for this swine pathogen. Histopathologically, the brain lesions were characterized by a lymphocytic leptomeningitis and a compression necrosis of the cerebral cortex.

Several foci of primarily oligodendrocytes adjacent to the lateral ventricle were present in both the control and the

infected animals, suggesting that this is a normal cellular accumulation in the brain of young pigs. Dublin (14) states that the accumulation of microglial cells adjacent to the ventricles of the brain in infants was considered at one time to indicate a neonatal form of encephalitis. Now these accumulations are considered normal.

When determining the etiology of field cases of meningitis in swine, M. hyorhinis should be considered. This contention is supported by the high percentage of recovery of M. hyorhinis from the cerebrospinal fluid at the early sampling periods, the presence of a meningitis in animal 34 and the common occurrence of M. hyorhinis in the respiratory tract of swine.

A comparison of the lesions which were observed in this study of pigs infected with M. hyorhinis to those reported for the swine disease referred to by various European workers as Glässer's disease is very difficult at this time. Many of these European workers were not aware that the M. hyorhinis organism existed.

In most instances the diagnosis of Glässer's disease was used when designating a polyserositis syndrome in pigs. Glässer et al., (22) and Hjärre and Wramby (27) reported that this syndrome was caused by Hemophilus influenzae suis. Both Glässer's disease and M. hyorhinis polyserositis affect pigs which are approximately the same age but the mortality rate is different. In M. hyorhinis infection the mortality rate is

very low. According to the description by Glässer et al.,
(22) and Hjärre and Wramby (27) Glässer's disease, as it
occurs in Europe, has a high mortality rate.

The gross lesions of the synovial membranes are very
similar in the two conditions. A histopathological evaluation
of the lesions of the synovial membrane in Glässer's disease
has not been reported. The brain lesions which are produced
by Glässer's disease are characterized by a neutrophilic lep-
tomeningitis, whereas in this study those produced by M. hyo-
rhinis consisted of a lymphocytic leptomeningitis.

With these differences in mind, it would seem advisable
to refer to the syndrome caused by M. hyorhinis as myco-
plasmosis. Until a study is conducted in Europe to determine
if M. hyorhinis is present in typical cases of Glässer's
disease, separate terminology for the 2 conditions should be
used.

Acute swine erysipelas arthritis could be confused some-
times with the arthritic lesions of mycoplasmosis. Sikes
et al., (63) and Collins and Goldie (8) state that the acute
lesions of swine erysipelas are characterized by vascular
engorgement and edema of the synovial membrane. Histopatho-
logically, there was initial lymphocytic infiltration and
proliferation of the synovial villi. Synovial membranes which
were acutely infected with M. hyorhinis were characterized by
hyperemia particularly those near the tips of the synovial
villi, and in some cases by fibrin formation on the synovial

membranes. Histopathologically, such synovial membranes evidence a diffuse infiltration of plasma cells and lymphocytes, hyperemia, swelling of the synovial cells and, occasionally, by fibrin formation on the luminal surface. When fibrin is present, a neutrophilic infiltration of the synovial villi occurs. Thus, the pathological changes of the acute phase of both swine erysipelas and mycoplasmosis arthritis are similar.

A comparison between the synovial membrane changes in chronic swine erysipelas described by Sikes et al., (62) and Collins and Goldie (8) and those observed in chronic M. hyorhinis infected pigs reveals that there is a definite difference in the degree of synovial villi hypertrophy. M. hyorhinis infection produces a synovial membrane which is velvet-like in appearance, whereas E. insidiosa produces a more polyp-like synovial villi. The highly vascularized connective tissue of the villi was not observed with M. hyorhinis arthritis and pericapsular fibrosis was minimal.

Both erysipelas arthritis and M. hyorhinis arthritis may produce a pannus formation of synovial membrane origin and osteoporosis probably resulting from disuse of affected limbs. However, pannus formation does not occur frequently in M. hyorhinis arthritis since it was observed in only one experimental pig. The osteomyelitis frequently caused by the swine erysipelas organism was not observed with M. hyorhinis infection.

Sikes et al., (62) report that the cells which are

present in the synovial fluid in swine erysipelas arthritis are primarily mononuclear cells, whereas the cellular components of the synovial fluid in M. hyorhinis arthritis are primarily neutrophiles.

The periarticular and bone marrow abcess formation and the articular surface erosion which occur with pyogenic arthritis were not observed in M. hyorhinis arthritis.

The gross and microscopic synovial membrane changes which were observed by Cordy (9) and Cordy et al., (10, 11) in the goat arthritis which was produced by Mycoplasma sp. closely resemble the alterations observed in M. hyorhinis arthritis of swine. The hyperemia and velvet-like proliferation of the synovial membrane are common in both conditions. Microscopically, both conditions exhibit hyperemia and infiltration of neutrophiles and lymphocytes into the synovial membrane in the acute stages. In the chronic phase of goat arthritis there is a proliferation of synovial cells and a perivascular mononuclear cuffing. These changes are also common to M. hyorhinis arthritis.

There is little similarity between the cellular changes reported by Sabin (54, 55, 56), Collier (7), Preston (51), Findlay et al., (18) and Ito et al., (30) in rats and mice which are affected with M. neurolyticum and M. arthritidis arthritis and swine which are affected with M. hyorhinis arthritis. The cellular changes associated with the former are suppurative in nature and in some instances there is actual

ankylosis of the joint.

The probable development of M. hyorhinis infection in experimental pigs inoculated intraperitoneally appears to be as follows. First, the M. hyorhinis organisms invade the blood stream with subsequent invasion of the pleura and peritoneum. In addition, the peritoneal involvement results from direct extension of the original inoculum. The organism manifests its action on the synovial membrane 2 or 3 days after the initial pleuritis and peritonitis has been established. The localization in and on the synovial membrane elicits an inflammatory cellular change consisting primarily of monocytes in the early stages. As the membrane becomes more acutely involved, fibrin formation occurs in association with an infiltration of neutrophiles. The irritative action of the organism remains and causes the synovial membrane and synovial cells to proliferate. An increased volume of synovial fluid results from the irritative action of the organism. A disruption in the orderly formation of the cartilage cells of the epiphyseal plate possibly caused by some metabolic change occurs in conjunction with the development of the visceral lesions. Other changes of osteoporosis occur at a later time from disuse or debilitation.

SUMMARY

1. Thirty-six pigs 3 weeks of age were divided into 6 groups of 6 pigs each.

2. Four pigs in each group were inoculated intraperitoneally with a 48-hour culture of M. hyorhinis, whereas 2 pigs served as uninoculated control animals. The groups were then necropsied at 4, 6, 10, 15, 30 and 56 days postinoculation.

3. Sixteen of 24 inoculated swine developed varying degrees of lameness at 5 to 12 days postinoculation. In some animals only 1 joint was involved, whereas in other animals as many as 5 joints were affected. The gross appearance of unopened involved joints varied from no visible alteration to a soft, fluctuating distention of the joint capsule.

4. The acute synovial membrane changes consisted of marked hyperemia, edema and in some cases fibrin deposits. Histopathologically, the acute synovial membrane changes are characterized by hyperemia, enlargement of the synovial cells, infiltration of plasma cells, mononuclear macrophages, a few lymphocytes and, occasionally, neutrophiles.

5. The chronic synovial membrane changes consisted of mild hyperemia and hypertrophy of the synovial villi associated with a yellowish coloration of the synovial membrane. Histopathologically, the chronic synovial membrane changes are characterized by hypertrophy of the synovial villi, hyperplasia of synovial cells and lymphocytic infiltrations which

were concentrated in nodular foci. A lymphocyte depletion of
the synovial villi was beginning by 56 days postinoculation.

6. The predominant cells which were present in the syno-
via were the neutrophiles which first appeared at 10 days
postinoculation. The synovia of the control animals remained
relatively acellular.

7. The pathological bone changes were first seen at 10
days postinoculation. These bone changes are characterized by
disorganization of the orderly maturation of the cartilage
cells in the vesicular zone of the epiphyseal plate. A
lattice-work-like trabeculae in the primary spongiosa resulted
from these changes in the epiphyseal plate. At 56 days post-
inoculation one joint was affected with initial fibrous anky-
losis as evidenced by a pannus formation. The pannus was
attached to the articular surface with subsequent metaplasia
of the cartilage to fibrous connective tissue. Changes typi-
cal of bone atrophy were observed in one animal. These were
due to disuse of the limb.

8. The thoracic and abdominal organs exhibited a
fibrino-purulent serositis. By 30 days postinoculation these
lesions had undergone organization with an adhesion formation
resulting. In the early stages this exudate consisted prima-
rily of fibrin and neutrophiles in association with a limited
number of macrophages and lymphocytes. The serosal membranes
exhibited swelling of the serosal cells accompanied by infil-
tration of plasma cells, macrophages and in some areas

neutrophiles. By 30 days postinoculation the inflammatory cells were primarily lymphocytes, isolated in foci in the sub-serosal membrane spaces. In each affected organ the inflammatory cellular changes extended inward a short distance from the serosal surface.

9. The serosal membrane changes extended into the scrotal cavity. In this region the changes resembled closely those seen in the other visceral organs. At 10 and 15 days postinoculation there was a peritubular infiltration of neutrophiles present in the testicle.

10. At 56 days postinoculation one pig had a turbid cerebrospinal fluid associated with hyperemia of the meningies. Histopathologically, there was a lymphocytic leptomeningitis present.

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